Neurology

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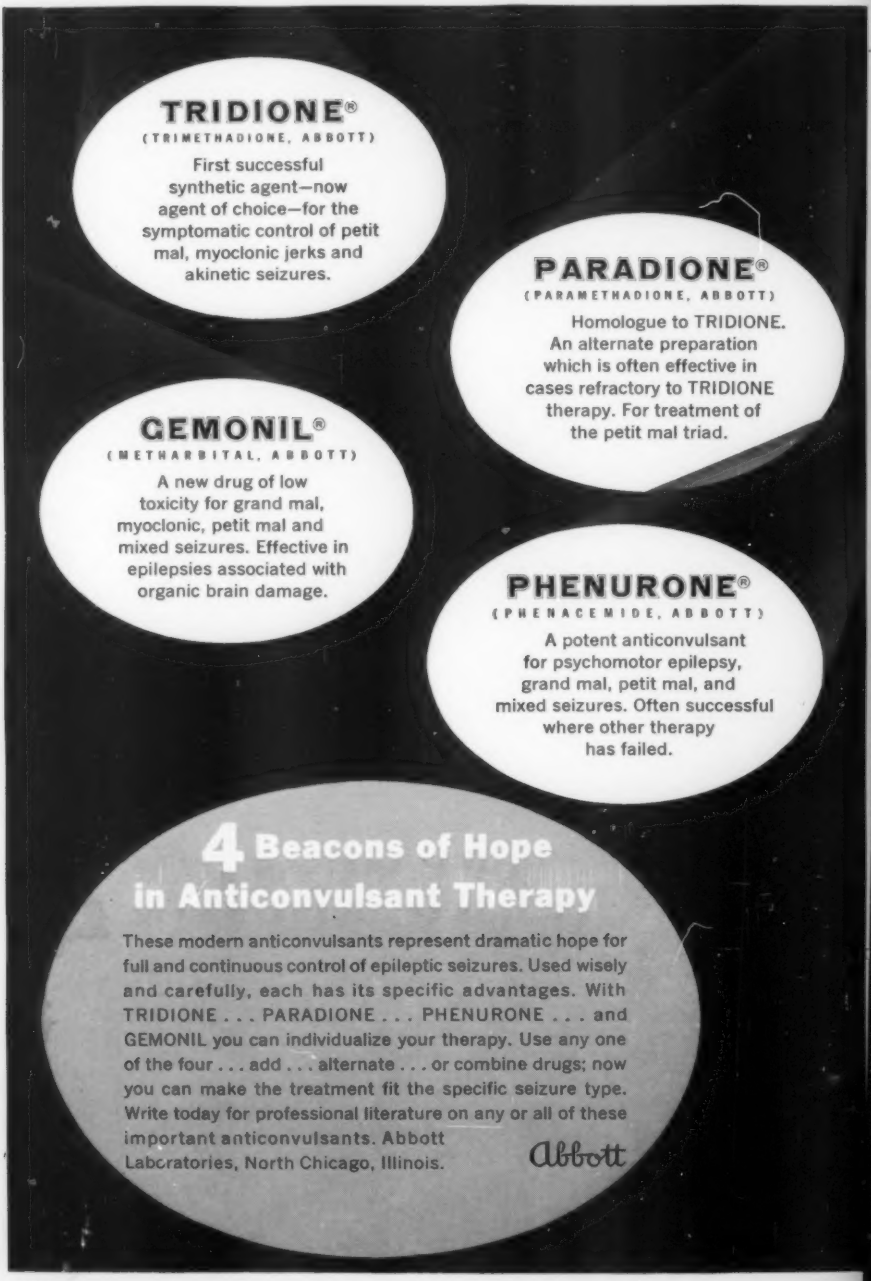
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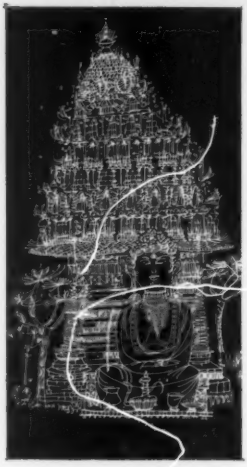

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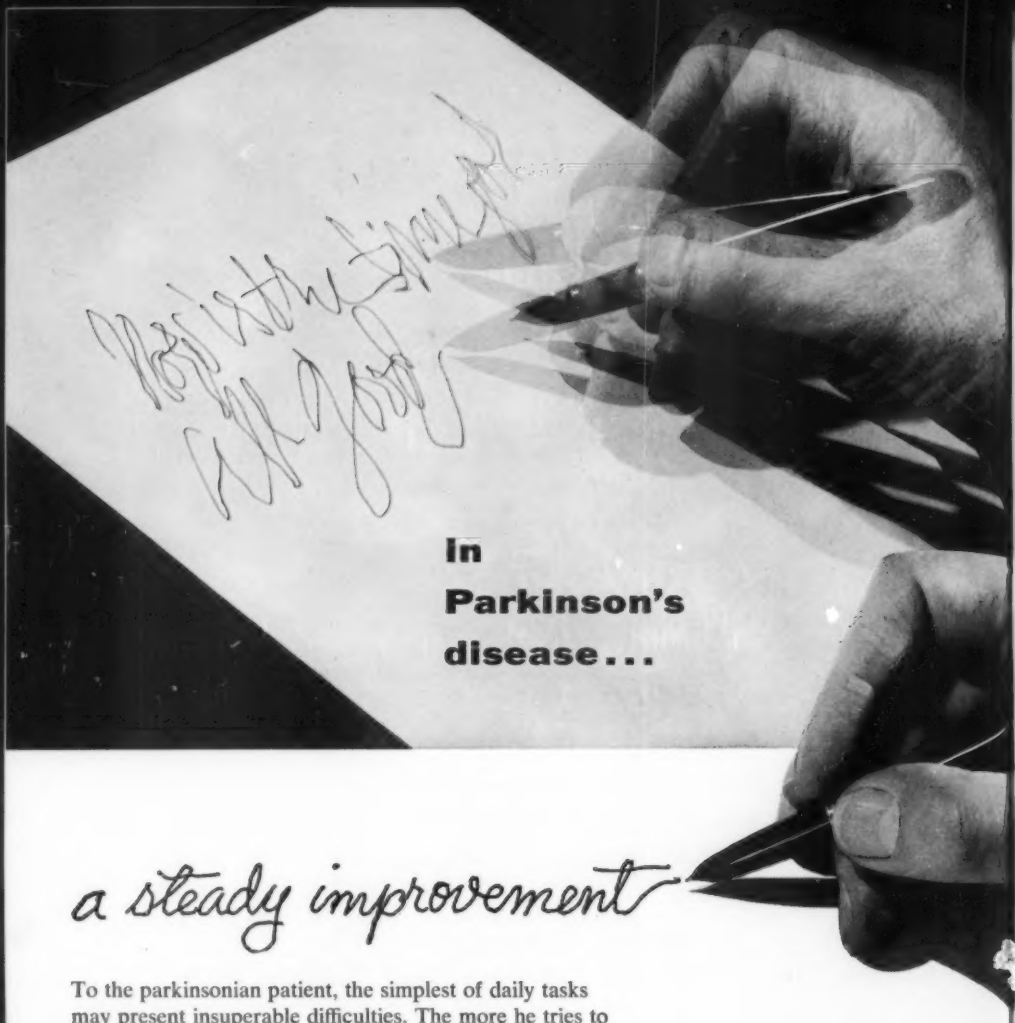

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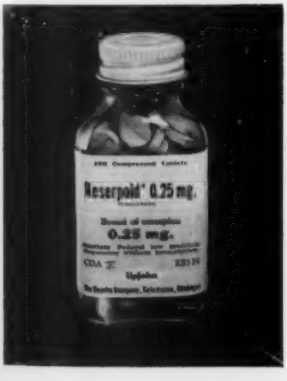

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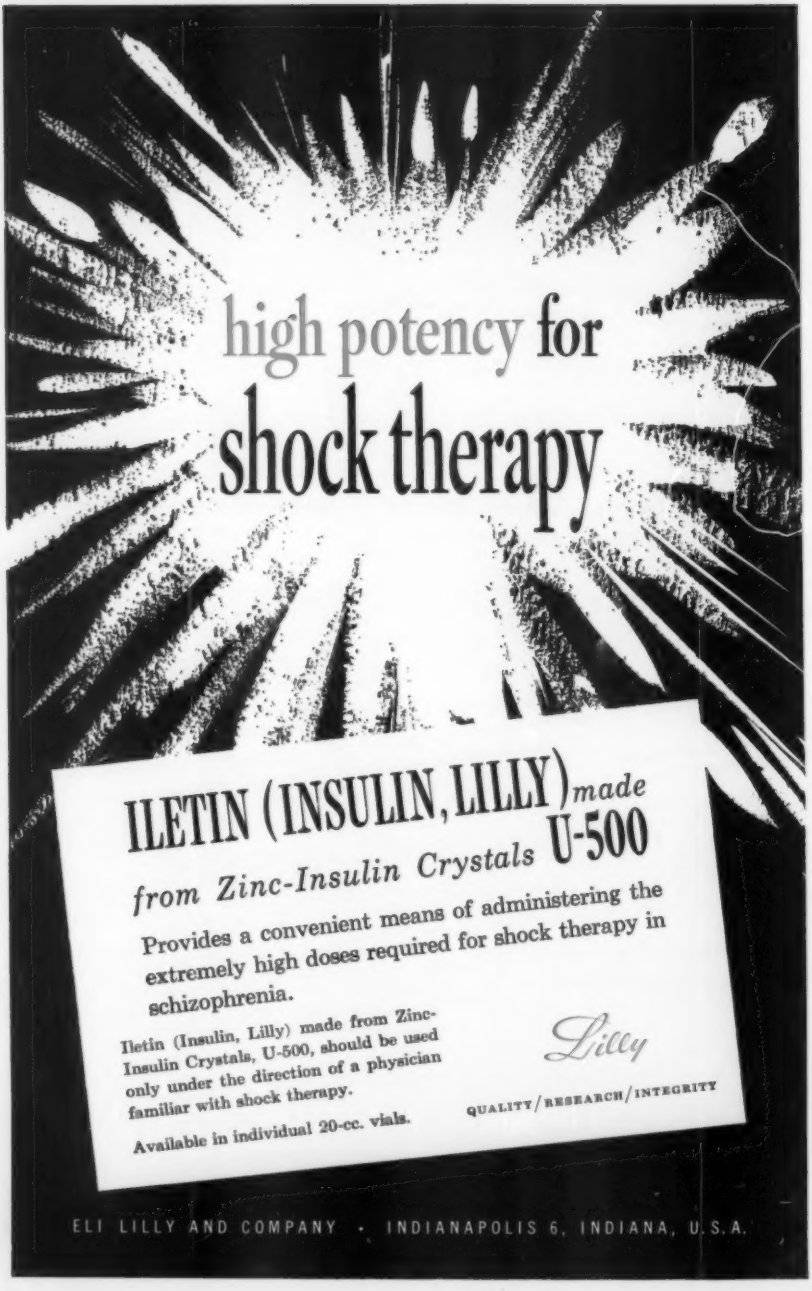
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Volume 5 Neurology Number 1

Combined Trigeminal and Glossopharyngeal Neuralgia

Richard J. Brzustowicz, M.D.

TRIGEMINAL and glossopharyngeal neuralgia are the two major types of neuralgia which produce paroxysmal attacks of pain in the face. Trigeminal neuralgia, or tic douloureux, is characterized by intermittent, sharp, shooting pain involving one, two, or all three branches of the trigeminal nerve. According to Krause,[1] this disease was first described by Avicenna about 1000 A.D. Lewy,[2] however, pointed out that the first clear description of trigeminal neuralgia was written in the last part of the seventeenth century by Fehr and Schmidt. Fothergill in 1773 characterized this disease as a "painful affection of the face."[3] The surgical treatment of trigeminal neuralgia can be traced to the beginning of the nineteenth century. It is known that Baillie[4] (1761-1823) divided the trigeminal nerve to relieve neuralgia and that Carnochan[5] in 1858 described a method of extracranial section of the maxillary and mandibular nerves. Carnochan's method for trigeminal neurectomy was supplanted by Hartley's[6] technic of intracranial section of the second and third divisions of the trigeminal nerve. At the turn of the century a number of surgeons described various methods for treating trigeminal neuralgia, but the modern operation for the radical treatment of this disease is based on the work of Frazier and Spiller,[7,8] who showed that section of the sensory root between the ganglion and the pons resulted in permanent anesthesia in the peripheral distribution of the trigeminal nerve and that regeneration of the fibers was impossible.

Glossopharyngeal neuralgia, which involves the ninth cranial nerve, is characterized by sharp, paroxysmal pain starting in the throat on one side and extending along the jaw to the ear. Weisenburg[9] described the symptoms of glosso-

Work presented in this paper was carried out under the direction of Dr. Frederick P. Moersch of the section of neurology, Mayo Clinic, Rochester, Minnesota, while Dr. Brzustowicz was a fellow in neurosurgery at the Mayo Foundation, University of Minnesota Graduate School.

pharyngeal neuralgia in a case in which necropsy revealed a tumor of the cerebellopontine angle which was pressing on the glossopharyngeal nerve. Sicard and Robineau[10] described glossopharyngeal neuralgia but were not certain that it was entirely due to the involvement of the ninth cranial nerve. Harris[11] also described glossopharyngeal neuralgia, and Doyle[12] in this country was the first to report four cases. Adson[13] was the first to section the glossopharyngeal nerve for the cure of this type of neuralgia. He at first tried the extracranial approach but then advocated the intracranial route for section of the nerve. Peet,[14] however, credited Dandy[15] with the first successful section of the ninth cranial nerve for glossopharyngeal neuralgia.

Trigeminal neuralgia occurs about 75 times more frequently than does glossopharyngeal neuralgia.[16] It usually appears after the age of 40 years. Women are affected more frequently than men. The right side is involved more often than the left. Rarely does the disease occur bilaterally at the same time, although it can first involve one side of the face and then the other. Glossopharyngeal neuralgia also has its greatest incidence among persons who are past 40. The sexes are affected about equally. The two sides are also affected about equally. The occurrence of glossopharyngeal and trigeminal neuralgia concurrently or sequentially is rare. In 1935, Peet[14] reported 14 cases of glossopharyngeal neuralgia and said that trigeminal neuralgia also was present in nine of the 14 cases.

The following data were obtained by reviewing cases of trigeminal and glossopharyngeal neuralgia observed at the Mayo Clinic. Approximately 200 cases of trigeminal neuralgia are observed each year at this institution. Thirty-four cases of glossopharyngeal neuralgia were observed in a period of 15 years, from 1935 to 1949 inclusive, about one case of glossopharyngeal neuralgia for every 88 cases of trigeminal neuralgia. Trigeminal neuralgia also was present in nine of the 34 cases of glossopharyngeal neuralgia. Of the nine patients with combined trigeminal and glossopharyngeal neuralgia, six were men and three were women. All were more than 40 years of age. The combined neuralgia affected the left side in seven cases and the right side in two cases.

Table 1 shows the sex of the patients and the side affected in 199 cases of trigeminal neuralgia and 34 cases of glossopharyngeal neuralgia. Clinical data in the nine cases of combined trigeminal

TABLE 1
SEX OF PATIENTS AND SITE OF AFFECTION IN 199 CASES OF TRIGEMINAL NEURALGIA AND 34 CASES OF GLOSSOPHARYNGEAL NEURALGIA

	Trigeminal neuralgia	*Glossopharyngeal neuralgia*
Sex:		
Males	82	14
Females	117	20
Site of affection:		
Left side	66	22
Right side	128	12
Both sides	5	–

TABLE 2

CLINICAL DATA IN CASES OF COMBINED TRIGEMINAL AND GLOSSOPHARYNGEAL NEURALGIA

Case	*Age*	*Sex*	*Sequence of occurrence of neuralgia*	*Side*	*Duration*	*Operation*
1	53	F	Third, second, and first divisions of trigeminal nerve	Right	21 yr.	—
			Glossopharyngeal nerve	Right	5½ yr.	—
2	54	F	Second and third divisions of trigeminal nerve	Left	7 yr.	—
			Glossopharyngeal nerve	Left	5 yr.	—
3	59	M	Second and third divisions of trigeminal nerve	Left	2 yr.	+
			Glossopharyngeal nerve	Left	1 yr.	+
4	41	F	Glossopharyngeal nerve	Left	3 mo.	+
			Third division of trigeminal nerve	Left	7 yr.	+
5	61	M	First, second, and third divisions of trigeminal nerve	Left	1½ yr.	+
			Glossopharyngeal nerve	Left	1 day(?)	+
6	53	M	Second and third divisions of trigeminal nerve	Left	10 yr.	+
			Glossopharyngeal nerve	Left	5 yr.	—
7	57	M	Second and third divisions of trigeminal nerve	Right	6 yr.	+
			Glossopharyngeal nerve	Right	3½ yr.	+
8	49	M	Second and third divisions of trigeminal nerve	Left	7 yr.	+
			Glossopharyngeal nerve	Left	3 mo.	—
9	41	M	Glossopharyngeal nerve	Left	7 yr.	+
			Third division of trigeminal nerve	Left	1 yr.	+

and glossopharyngeal neuralgia are presented in table 2. Table 3 shows the age of the patients by decades in the cases of trigeminal neuralgia, glossopharyngeal neuralgia, and combined trigeminal and glossopharyngeal neuralgia.

REPORT OF CASES

The nine cases of combined trigeminal and glossopharyngeal neuralgia will be reported briefly.

Case 1.—A 53 year old woman complained of sharp, shooting pain in the right side of the

TABLE 3

AGE OF PATIENTS

Age	*Trigeminal neuralgia* (199 cases)	*Glossopharyngeal neuralgia* (34 cases)	*Combined trigeminal and glossopharyngeal neuralgia* (9 cases)
20 to 29	4	–	–
30 to 39	16	5	–
40 to 49	28	8	3
50 to 59	58	8	5
60 to 69	53	8	1
70 to 79	32	5	–
80 to 89	6	–	–

lower jaw, in the teeth in this portion of the jaw, and in the right side of the face. The pain had occurred each spring and winter for about 14 years. For two years pain had also occurred in the right side of the upper jaw, in the right side of the palate, and above the right eye. A definite trigger zone was present in the lower part of the right cheek. An alcohol block was recommended but was refused by the patient.

The patient was next seen seven years later. In addition to pain in the entire right side of the face, in the right side of the lower jaw, and the right side of the tongue, she then complained of sharp, intermittent attacks of pain "deep inside" the right side of the neck. She was unable to swallow food without experiencing a spasm of pain. Section of the trigeminal and glossopharyngeal nerves on the right side was recommended, but the patient decided to postpone the operation until some future date.

Case 2.—A 54 year old woman complained of severe, intermittent attacks of pain deep in the left ear. She had had attacks of sharp pain in the left side of the face for about seven years. Pain had begun in the left cheek and extended back to the left ear. The facial pain gradually subsided, but the pain in the ear persisted and was brought on by swallowing of solid food or fluids. When the patient was first observed the pain was mild, and she was instructed to return if the pain became severe.

She returned four years later and said that drinking cold water produced a sharp, severe pain in the left side of her throat and that the pain extended to the left ear. Cocainization of the left tonsillar fossa permitted the patient to eat a hearty meal. Section of the left glossopharyngeal nerve was recommended but the patient decided to postpone the operation.

Case 3.—A 59 year old man had had severe pain in the left cheek and in the left side of the upper lip for two years. Injection of alcohol into the second division of the left trigeminal nerve produced considerable relief. Subsequently the sensory root of the trigeminal nerve was sectioned.

The patient returned a year later. At that time he complained of sharp pain in the left side of the throat, precipitated by swallowing. Cocainization of the tonsillar fossa on the left side relieved the pain. Section of the left glossopharyngeal nerve produced complete relief.

Case 4.—A 41 year old woman came to the clinic in June 1927. About three months previously, she had noted sharp, spasmodic pain in the left side of the lower jaw. The pain was brought on by talking, and by chewing or swallowing food. It extended along the jaw to a point just in front of the left ear. Section of the left glossopharyngeal nerve relieved the pain.

In 1941 the patient returned to the clinic because of spasms of pain in the left side of the lower jaw, in the left side of the face, and in the left side of the temple. The pain had been present for about seven weeks, and was more severe in the jaw than in the face and temple. Injection of alcohol into the third division of the left trigeminal nerve produced prompt relief.

When the patient returned for a checkup in 1945, she was having only mild pain along the distribution of the third division of the left trigeminal nerve. She returned in 1948 because of recurrence of pain of increased severity in the left side of the lower jaw and in the left side of the face. Section of the sensory root of the left trigeminal nerve produced prompt relief.

Case 5.—A 61 year old man had had pain along the distribution of all three divisions of the left trigeminal nerve for about 15 months. The pain was sharp and intermittent, and it was brought on by talking, eating, or touching the side of the face. For 24 hours before the patient first was observed at the clinic, he had had excruciating pain in the left side of the throat. The pain extended to the left ear, and the patient was unable to swallow either solid food or liquids. Cocainization of the throat relieved the pain promptly. Subsequent section of the left glossopharyngeal nerve produced a good result. Nine days after operation the patient began to have sharp, shooting pain in the left side of the lower lip, in the left side of the lower jaw, and in the gums in this portion of the jaw. The posterior root of the trigeminal nerve was sectioned. When the patient was dismissed, he felt well and could eat without any discomfort.

Case 6.—A 53 year old man had had pain in the left side of the face for about seven years. The pain had first occurred in the left side of the lower jaw, but it subsequently occurred in the left cheek and in the left side of the temple. Two years after the onset of pain, the

patient began to have sharp pain in the left side of the throat. This pain was brought on by swallowing and did not occur at the same time as the pain in the face. Since the patient complained primarily of pain in the face and not of pain in the throat when he first was observed at the clinic, alcohol was injected into the second and third divisions of the left trigeminal nerve. The patient subsequently was free of pain for three years. At the end of that period he returned to the clinic because of severe pain in the left side of the lower jaw and in the left side of the face. Section of the left trigeminal nerve produced a good result.

Case 7.—A 57 year old man came to the clinic in 1943 because of pain which had been present in the right side of the face for six years. A severe paroxysm of pain had occurred deep in the right ear in 1933, and a diagnosis of mastoiditis had been made. Subsequently the pain in the ear decreased in severity, and he began to have paroxysmal attacks of pain which was situated along the right side of the lower jaw and extended toward the nose. Acute attacks of pain were brought on by yawning, chewing, or sneezing. In 1940 the pain increased in severity in the right side of the face, in the right ear, and under the right side of the lower jaw. Incomplete section of the right trigeminal nerve was performed in 1942, alleviating the facial pain, but the pain along the right side of the lower jaw persisted. In 1943 the right glossopharyngeal nerve and the sensory root of the right trigeminal nerve were sectioned. This operative procedure relieved the pain completely.

Case 8.—A 49 year old man came to the clinic in 1936 because of pain which had been present in the left side of the face for seven years. The pain had begun in front of the left ear and extended to the left side of the upper and lower jaws, to the left side of the nose, and to the left side of the upper lip. It was brought on by talking or eating. Alcohol had been injected into the left gasserian ganglion in 1931 and again in 1935. On each occasion this treatment relieved the pain for about ten months. In 1936 the pain recurred along the distribution of the second and third divisions of the left trigeminal nerve. Section of the sensory root of the left trigeminal nerve produced complete relief. In 1938 the patient returned because of sharp shooting pain which had been present at the left side of the root of the tongue and in the left side of the throat for about three months. The pain was brought on by coughing, drinking water, or stretching the neck. Cocainization of the left tonsillar region relieved the pain. Section of the left glossopharyngeal nerve was recommended, but the patient decided to postpone the operation.

Case 9.—A 41 year old man had had sharp, intermittent pain in the left side of the throat for seven years, precipitated by drinking water or by swallowing food. It extended along the left side of the neck to the left ear. The left tonsillar fossa was cocainized, and the patient then was able to drink fluids without any pain. Section of the left glossopharyngeal nerve relieved the pain completely. Two years later the patient returned complaining of severe pain in the left side of the base of the tongue. There was some extension of pain into the neck. The lingual branch of the left trigeminal nerve and the left descending hypoglossal nerve were sectioned. The patient continued to have some pain in the left side of the base of the tongue although the sharp spasms of pain disappeared.

DIFFERENTIAL DIAGNOSIS

Neuralgia of the third division of the trigeminal nerve is difficult to distinguish from glossopharyngeal neuralgia, as is illustrated by the nine cases reported here. The character and duration of pain in both types of neuralgia are the same, but the distribution is different. In cases of glossopharyngeal neuralgia, the trigger zone is in the tonsillar fossa and pain can be brought on by yawning or swallowing either solid foods or fluids. The pain extends from the region of the tonsillar fossa and pharynx deep in the neck to the ear. The pain is not brought on by touching or rubbing any part of the face. Cocainization of the tonsillar fossa will temporarily stop the acute attacks of pain. If the pain is due to neuralgia of the third division of the trigeminal nerve, cocainization of the tonsillar fossa will have no effect. Similarly, injection of alcohol into the third division of the trigeminal nerve will not af-

fect the paroxysms of pain deep in the neck due to glossopharyngeal neuralgia. It is possible for neuralgia involving the third division of the trigeminal nerve and glossopharyngeal neuralgia to exist concurrently, but one usually precedes the other. In three of the five cases reported by Peet,[14] the paroxysms began along the distribution of the trigeminal nerve; in the two remaining cases, they began along the distribution of the glossopharyngeal nerve. In seven of the nine cases reported in this paper, the neuralgia began along the distribution of the trigeminal nerve; in the two remaining cases, it began along the distribution of the glossopharyngeal nerve.

ANATOMIC BASIS FOR COMBINED TRIGEMINAL AND GLOSSOPHARYNGEAL NEURALGIA

The cause of either trigeminal or glossopharyngeal neuralgia is not definitely known. Because of their more frequent occurrence, cases of trigeminal neuralgia have been studied thoroughly, and various ideas have been advanced as to the cause of the intermittent, cyclic pain. There is some evidence which indicates that trigeminal neuralgia may be due to vasospastic ischemia.[17] Presumably, the same cause would have to be postulated for glossopharyngeal neuralgia.

Even though the exact mechanism producing paroxysmal pain in trigeminal and glossopharyngeal neuralgia is not known, the reasons for the combined occurrence of these two types of neuralgia can be understood by reviewing the anatomic distribution of pain fibers in the trigeminal and glossopharyngeal nerves.

The nerves supplying the structures derived from the branchial arches are the trigeminal, facial, glossopharyngeal, and the vagus-spinal accessory complex.[18] Of these, the trigeminal nerve is the chief sensory nerve of the face. Brodal[19] has pointed out that the facial, glossopharyngeal, and vagus nerves also have some somatic representation, a factor of definite clinical significance.

The modalities of pain and temperature are mediated by the afferent fibers of neurons having their cell bodies in the semilunar or gasserian ganglion. Centrally, as soon as the axons of these cells bifurcate they enter the pons in a short ascending branch and a long descending branch (figure 1).[18,20] The short ascending branch terminates almost immediately in the main sensory trigeminal nucleus. The descending branch forms the descending or spinal tract of the trigeminal nerve. It descends in the pons and medulla down to the cervical region and becomes continuous with Lissauer's tract.[21] The descending fibers terminate in the nucleus of the spinal tract of the trigeminal nerve, which lies medial to the tract. The secondary trigeminal fibers arise from the main sensory nucleus and the nucleus of the spinal tract of the trigeminal nerve. The fibers arising from the latter nucleus, mediating chiefly pain and temperature, cross to the opposite side of the medulla and ascend near the ventromedial part of the medial lemniscus. In the pons, these fibers, known as the "trigeminal lemniscus," shift laterally and lie near the spinothalamic tract, which carries pain and temperature fibers from the body. Fibers arising from the main sensory nucleus and probably some from the nucleus of the spinal tract mediate touch and pressure. These fibers cross to the other side of the medulla and ascend near the dorsomedial surface of the medial lemniscus as the secondary trigeminal tract. All of the trigeminothalamic fibers from both

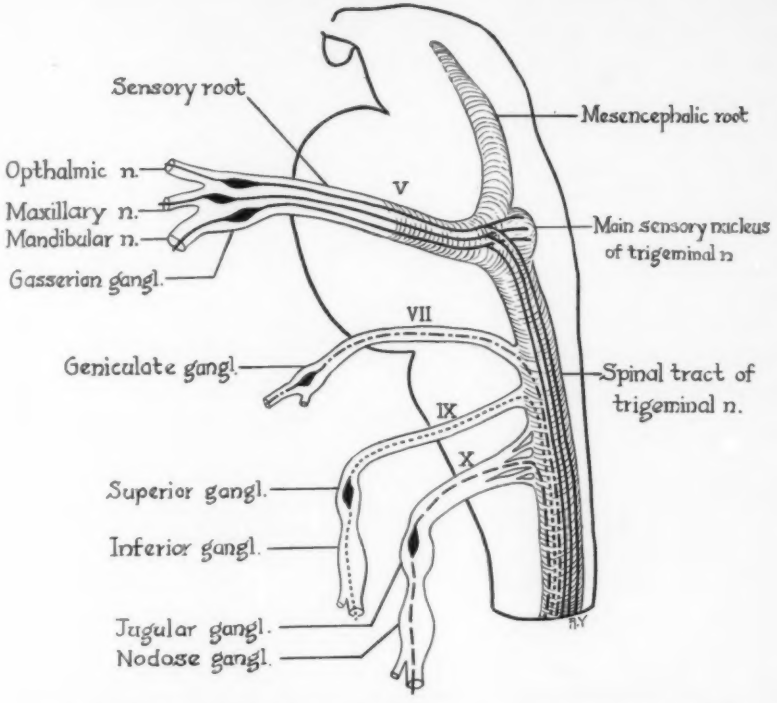

FIG. 1. Schematic representation of the somesthetic components of the seventh, ninth, and tenth cranial nerves and their relation to the trigeminal system.

the trigeminal lemniscus and the secondary trigeminal tract end in the posteromedial ventral nucleus of the thalamus. Thalamocortical fibers constituting the tertiary neuron then project to the postcentral gyrus.

The fibers in the spinal tract of the trigeminal nerve are arranged according to the representation of the three divisions of the nerve, rather than according to the representation of concentric zones converging on the oral and nasal orifices, as some authors believe.[21] The fibers representing the ophthalmic division are placed most ventrally in the spinal tract, while those of the mandibular division are placed most dorsally. The fibers from the three divisions descend to different levels. The ophthalmic fibers descend to the most caudal levels, some reaching as far as the second cervical segment. The maxillary fibers descend to the caudal end of the medulla, while the mandibular fibers descend to about the level of the dorsal nucleus of the vagus.

Since the facial, glossopharyngeal, and vagus nerves contain somatic afferent fibers which end in the nucleus of the spinal tract of the trigeminal nerve,

Krieg[18] suggested that this tract should be rightly called the "cranial somesthetic tract." Comparative anatomists[22,23] have shown that the trigeminal, facial, glossopharyngeal, and vagus nerves all supply structures derived from branchial arches. It is reasonable, therefore, that the somatic afferent fibers from these nerves should join the spinal tract of the trigeminal nerve. Brodal[19] studied several patients who had undergone a trigeminal tractotomy for tic douloureux (Sjöqvist procedure). He found that the distribution of anesthesia following tractotomy was greater than the area of known sensory distribution of the trigeminal nerve. In these patients, in addition to the anesthesia of the face, there was anesthesia in the distribution of the glossopharyngeal nerve (posterior third of the tongue, soft palate, and tonsillar fossa) and in certain parts of the ear which represented the somatic distribution from the facial and vagus nerves. Brodal felt that, since the somatic sensory fibers from the trigeminal, facial, glossopharyngeal, and vagus nerves descend together in the spinal tract of the trigeminal nerve, tractotomy could be used in the treatment of not only trigeminal neuralgia but also glossopharyngeal and facial neuralgia.

The anatomic relationship of the pain fibers in the trigeminal, facial, glossopharyngeal, and vagus nerves provides some help in establishing the probable cause and site of neuralgia involving these nerves. Adson,[16] in discussing possible causes for these types of neuralgia, pointed out that they occurred in persons who were past 40 years of age. He felt that this suggested sclerotic changes in the vessels supplying certain cerebral centers, thereby altering the function of the upper neurons of these nerves. Wolff[24] also believed that vascular changes were responsible for the occurrence of these types of neuralgia, but said that in trigeminal neuralgia, for example, the site of the defective circulation occurs either in the gasserian ganglion, the sensory root, or the nerves. He pointed out that "it is difficult to conceive of a central defect in circulation so circumscribed as to affect the function of only the trigeminal cells without involving adjacent nuclei and tracts. Also, such a defect must be so discrete as to produce pain limited to one or another division of the fifth cranial nerve."[24]

If a central site of ischemia in the trigeminal tracts or nuclei is postulated as a cause for trigeminal neuralgia, it could explain the occurrence of combined neuralgias. However, if this were the case, glossopharyngeal neuralgia should occur much more than one seventy-fifth as frequently as trigeminal neuralgia, because the somatic afferent fibers from the glossopharyngeal nerve descend with those of the trigeminal nerve in the spinal tract. It is difficult to see how fibers of the trigeminal system could be selectively affected without involving the fibers of the other cranial nerves in this somesthetic system. It is, therefore, more plausible to ascribe trigeminal neuralgia to a peripheral ischemic mechanism, affecting either the nerves, ganglion, or sensory root of the trigeminal nerve. A similar mechanism would have to be postulated for neuralgia involving the facial, glossopharyngeal, or vagus nerves either singly or in combination.

TREATMENT

The treatment of trigeminal neuralgia is either palliative or radical. The palliative measures consist of injection of

alcohol into the branches of the trigeminal nerve, or other medication. The radical treatment consists of a partial or complete section of the sensory root of the trigeminal nerve, either through a temporal approach or by a suboccipital approach as advocated by Dandy.[25] Sjöqvist[26] has advocated tractotomy or sectioning the spinal tract of the trigeminal nerve on the lateral surface of the medulla. More recently, Taarnhøj[27] has proposed decompression of the gasserian ganglion and the sensory root for trigeminal neuralgia, without sectioning the root. This procedure would have the obvious advantage of relieving the neuralgia without sacrificing sensation.

Glossopharyngeal neuralgia cannot be treated by the injection of alcohol into the nerve. If medication fails to relieve the paroxysms of pain, radical treatment is indicated. This consists of sectioning the glossopharyngeal nerve by using a suboccipital approach.[13,28]

If a combined trigeminal and glossopharyngeal neuralgia is present, it would seem that the operation of choice would be the trigeminal tractotomy of Sjöqvist. In this way, one procedure would produce anesthesia in the distribution of the entire somesthetic system of the head on the side incised. Similarly, bilateral trigeminal neuralgia could be treated by sectioning the descending spinal tract on both sides of the medulla at one operation.

SUMMARY

Trigeminal and glossopharyngeal neuralgias are painful and disabling. They usually occur after the age of 40 years. Trigeminal neuralgia occurs about 75 times as often as does glossopharyngeal neuralgia. The differential diagnosis of these two types of neuralgia is often difficult. Occasionally, they may occur concurrently. Rarely, trigeminal neuralgia may occur bilaterally. In a series of 34 cases of glossopharyngeal neuralgia observed at the Mayo Clinic between 1935 and 1950, combined trigeminal and glossopharyngeal neuralgia occurred in nine. Three women and six men were affected. All were more than 40 years of age. In seven cases trigeminal neuralgia occurred first, followed by glossopharyngeal neuralgia. In two cases, glossopharyngeal neuralgia occurred first. The combined neuralgia was present on the right side in two cases and on the left side in seven cases. Surgical treatment was used in seven of the nine cases.

From the anatomic point of view, fibers of the gasserian ganglion cells descending in the pons and medulla as the spinal tract of the trigeminal nerve are joined by somatic afferent fibers from the facial, glossopharyngeal, and vagus nerves. Secondary fibers from the nucleus of the spinal tract decussate and project to the posteromedial ventral nucleus of the thalamus. Fibers from the thalamus then project to the cortex of the postcentral gyrus. The present study favors Wolff's concept of a peripheral ischemia in the nerves, ganglion, or sensory root as a cause for trigeminal neuralgia. The current surgical treatment of trigeminal neuralgia includes section of the sensory root of the trigeminal nerve either by the transtemporal or suboccipital approach, or the trigeminal tractotomy of Sjöqvist. The surgical treatment of glossopharyngeal neuralgia consists of section of the glossopharyngeal nerve by means of a suboccipital approach.

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Observations on the Motor System following Cerebral Hemispherectomy

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THE PURPOSE of this report is to present observations on the effect of cerebral hemispherectomy on motor function. The material presented is part of a study pursued in an attempt to alleviate intractable convulsive seizures in a group of eight patients who have had seizures associated with a spastic hemiparesis or hemiplegia. These data must, therefore, be interpreted with regard for the fact that motor function was not normal preoperatively. All patients had become hemiparetic many years previously, most of them in very early life. That this influences the final results of hemispherectomy in this series of patients cannot be disregarded. To emphasize this one need only review the data collected and presented by Bucy[1] in 1944 and subsequently by others.[2,3] Because of these factors, the authors feel justified in presenting only the observations and not attempting a definitive interpretation, at least at this time.

It has been reported previously that the effect of unilateral cerebral hemispherectomy on the motor function of patients suffering from infantile hemiplegia is considerably different from that expected to follow such a radical procedure.[2,3,4] When the area of the brain that is presumed to affect motor control of the body is destroyed in adults through disease processes or surgical removal, a severe lasting hemiplegia occurs. In such patients, there is no recovery of function in the arm and little if any return of useful function in the leg. With similar lesions in patients who suffer hemiplegia in infancy or early childhood, comparable motor deficits do not occur. Seven of the eight patients in this series had become hemiplegic in infancy or early childhood and, although they were able to walk, all had some spastic deformity of the involved side, most marked in the upper extremity. The affected arms were useless except for gross movements of the shoulders and elbow joints. In four patients, however, movements at these joints were very strong. Three patients had some degree of movement in the fingers and in one patient this finger movement was adequate to be of assistance in dressing and undressing himself. There was mod-

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erate to severe atrophy of the muscles of the affected side in all patients. Deep tendon reflexes were extremely hyperactive and clonus was present in the knee and ankle. The abdominal reflexes were diminished to absent and the toe signs were positive in all patients.

The amount of cerebral tissue excised at the time of surgery varied slightly from patient to patient. At the time of excision the middle cerebral artery was cut at a distance of 1½ cm. from its origin from the carotid artery, and the anterior cerebral artery was sectioned just distal to the origin of the anterior communicating artery. The posterior cerebral artery was cut 1 cm. distal to its origin from the posterior communicating artery. An incision was then made longitudinally through the corpus callosum and the lateral ventricle was entered. The incision was continued at the lateral recess of the lateral ventricle just above and lateral to the caudate nucleus. It was then carried down through the internal capsule to emerge on the medial aspect of the temporal lobe, that is, along the incisura tentorii. With this incision it was felt that all the cerebral cortex, the corona radiata, and the basal nuclei lying lateral to the internal capsule including a portion of the caudate nucleus was removed. This included the hippocampal gyrus. Then by means of suction the caudate nucleus itself was removed. The variation in the amount removed from patient to patient consisted of leaving the caudate nucleus and part of the hippocampus in the first two patients undergoing the operation. Subsequently this tissue has also been removed.

Within an hour following completion of the operative procedure all patients had recovered sufficiently from the anesthesia to permit testing. At this time most of them could make gross movements with both the arm and leg. The previously spastic extremities were completely flaccid, but the reflexes and toe signs were still hyperactive. Within one week, two patients were walking unassisted and the other six were doing so within two to four weeks postoperatively. The average time required to regain walking ability was 12 days. This, of course, was greatly influenced by the patients' general postoperative state as well as the degree of physical rehabilitation. In the later four cases it was apparent that sufficient strength for standing unassisted and walking returned as early as the third to fifth postoperative day. Examination four months following operation showed that all but one patient had regained at least preoperative walking ability. In one patient this ability was considerably improved over the preoperative state.

FIG. 1. Drawing revealing extent of excision in hemispherectomy. Shaded area from A through B excised.

Ability to use the affected arm also returned to the preoperative level, but arm function returned somewhat more

slowly than did leg function. Finger movement was not abolished by hemispherectomy. All patients were able to move each of their fingers voluntarily. It was noted that the fingers could be moved with greater facility than the thumb. One of the more intelligent of the patients made the observation that postoperatively he could use his hand and arm without purposely thinking about it, as was necessary preoperatively. The fingers, however, were moved in a rather spastic attitude. One patient with a Sturge-Weber syndrome, in addition to a severe spastic hemiparesis, had marked athetoid movements of the involved arm and almost continuous bobbing movements of the head. Both these movements completely disappeared immediately following hemispherectomy. In two patients, orthopedic deformities became more apparent following surgery. With the initial lessening of spasticity of the extremities, unstable joints have increased movement; in these two patients an arthrodesis will probably be necessary.

The immediate postoperative state of the affected side, as mentioned above, was one of complete flaccidity even though the reflexes remained very hyperactive. Clonus was present and the toe signs were positive. As motor activity returned the affected side became more spastic, and in a period varying from one to nine months the spasticity was comparable to the preoperative level. In no case, however, was the spasticity more apparent than before surgery.

It has long been believed that abdominal reflexes are abolished by lesions of the premotor cortex. In this series all patients recovered some degree of activity in the contralateral abdominal reflexes. In two patients the reflexes had returned to normal within seven days postoperatively; in the others the abdominal reflexes had returned and were equal bilaterally by four months postoperatively.

In the beginning of this series only severe cases of hemiplegia were chosen to avoid causing further motor deficit. This initial trepidation has been completely unfounded and in the last few patients of this series the degree of preoperative hemiparesis has been relatively minimal. In these latter cases the postoperative neurologic status was good enough to permit the patients to do almost anything other children of their age could do. The effect of removal of the entire cerebral cortex as well as most of the basal ganglia did not result in any exaggeration of motor deficit even though the preoperative motor deficit was fairly minimal. Krynauw believed that the integrity of the caudate nucleus on the side opposite the hemiplegia was necessary for maintenance of preoperative motor function. This appeared not to be the case since four of the patients in this series had the caudate nucleus completely removed and they recovered motor function comparable to, if not to a greater extent than, the others.

CASE REPORT

A boy born April 15, 1938 sustained a severe head injury shortly after birth. At the age of three months grand mal type convulsive seizures began, and shortly thereafter weakness of the right arm and leg was observed. His general physical development was retarded, and by the age of four years he was extremely destructive and subject to violent temper tantrums. He was committed to a state institution for children in 1948 because of his personality aberration in addition to the recurrent convulsive seizures. Since that time he has had from 65 to 160 grand mal seizures a year, in spite of massive doses of anticonvulsants.

Preoperative examination revealed a well developed and well nourished boy with an obvious spastic right hemiplegia. He was cooperative but obviously retarded mentally. A measured intelligence quotient was 86. He had a right homonymous hemianopsia. There was severe bilateral and horizontal nystagmus, a central type seventh nerve paralysis, and a right spastic hemiparesis. There was moderate atrophy of the entire right side of his body. There was good muscle strength in the right shoulder and elbow and the right leg was very strong. He could feel all modalities of sensation but the response to such stimuli was slow. There was a very pronounced right hyperreflexia, normal abdominal reflexes, and a positive Babinski sign on the right. There was hemiatrophy of the left side of the skull. Carotid angiography revealed lack of filling of the middle cerebral artery.

On November 28, 1953 a left cerebral hemispherectomy was performed. The lowest level of section included the caudate nucleus. The first postoperative day he could move his right leg but not his arm. His speech was normal. On the second postoperative day he moved the right leg very well and his abdominal reflexes were normal bilaterally. He still could not move his right arm. The pain sensation appeared to be equal bilaterally. There was a marked hyperreflexia and positive toe signs on the right. On the third postoperative day he was able to move the right arm and very minimally the fingers of the right hand. On the fifth postoperative day he could stand alone, and on the seventh postoperative day his gait was equal to the preoperative level. At this time he was also able to move his right arm at the shoulder and elbow. He could move his right wrist and could make very purposeful and distinct movements with the fingers and thumb of the right hand. Examination six months postoperatively revealed that he had no seizures and was fully equal to his preoperative motor level. Except for fine work with his fingers, he could accomplish most physical feats of a boy his age.

SUMMARY

The effects of cerebral hemispherectomy on the motor function in a series of eight patients with intractable convulsive seizures and hemiparesis occurring at an early age in life are reported. There seems to be no permanent deficit in motor function produced by this operative procedure. The caudate nucleus does not seem to be necessary for the integrity of the motor function of the contralateral extremities. Immediately postoperative the involved extremities are flaccid, but over a period of many months they again become spastic comparable to their preoperative status. Abdominal reflexes are not abolished by hemispherectomy. It is believed that the rapid return of motor function to the preoperative level is due to the contralateral hemisphere having assumed the function of the pathologic side many years preoperatively. It is felt that the pathologic hemisphere offers only a restraining effect on the motor function of the normal side.

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Hereditary Sensory Neuropathy

Irving H. Heller, M.D. and Preston Robb, M.D.

RECENTLY the opportunity arose to study a group of patients with the characteristics of an interesting neurologic syndrome, hereditary sensory neuropathy. In general they showed, in varying degrees, loss of deep tendon reflexes, loss of all sensory modalities over the extremities in stocking and glove distribution, and severe trophic disorders in all four extremities. The profound reflex changes, sensory loss, and trophic disturbances were not associated with any motor weakness or muscular atrophy. We have considered these cases as part of a group which was originally described as hereditary perforating ulcers of the feet, and have since been reclassified as hereditary sensory neuropathy.

In 1852 Nélaton[1] gave what was probably the first published report of perforating ulcers of the feet. At that time he felt that the disorder was one arising primarily in the bones. Many cases have been reported since the turn of the century. Bruns,[2] Clarke and Groves,[3] Price,[4] Schultze,[5] and Wagner[6] felt their cases were due to lumbosacral syringomyelia, while Riley,[7] Enderle,[8] Tocantins and Riemann,[9] Göbell and Runge,[10] and Weitz[11] favored status dysraphicus.

In 1929 Guillain and Thévenard[12] reported two siblings whose father, brother, and sister had died of a similar disease. The earliest age of onset in this family was 13 and the latest was 39. Thévenard and Coste[13] in 1935 reported two additional cases from a different family. These patients had loss of pain and temperature sensation over the distal portions of the feet, with touch only slightly impaired. Position and vibration sense were intact. The deep tendon reflexes remained intact until late in the disease when the ankle jerks were reported diminished. Over the subsequent years pain developed in the lower limbs, with trophic ulcerations of the feet necessitating amputation. The upper extremities were practically all spared. There was one exception, a patient who had ulcerations of the hand and diminished biceps and triceps reflexes. In the 1929 and 1935 publications the authors favored the diagnosis of familial lumbosacral syringomyelia, but Thévenard[14] reported a follow-up in 1942, coming to no definite conclusion other than a descriptive term "acropathie ulcero-mutilante familiale." Thévenard and his associates thus denoted the syndrome as one occurring near puberty (earliest onset in their review of the literature was eight years of age), usually affecting only the lower limbs, with peripheral sensory

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loss to pain and temperature and occasionally to all forms of sensation, with diminished or absent deep tendon reflexes, and trophic ulcerations. Muscular atrophy was not a part of the syndrome.

In 1945 Parks and Staples[15] described two patients, one aged two and the other aged eight, who developed glove and stocking sensory loss to all forms of sensation, touch being the most severely affected, position and vibration less so, with loss of deep tendon reflexes, and trophic ulcerations of the fingers and hands. The youngest had diminished corneal reflexes and hypalgesia over the face; the other had some weakness but no obvious atrophy of muscles of the hands and feet. They reviewed seven cases previously reported under the name of Morvan's disease, which, with minor variations, they felt resembled their own patients. These included those reported by Head,[16] Bousquet,[17] Barbier and Jarricot,[18] Cruchet and co-workers,[19] Wagner,[6] and Gaté and Riou.[20] Parks and Staples felt that the correct diagnosis was a peripheral neuropathy of sensory type.

In 1946 Ogryzlo[21] reported four cases in one family who had varying degrees of the same syndrome with early onset in infancy and with a progressive course, eventually requiring amputation of one or other leg due to severe ulcerations. Sections of nerves obtained from amputated limbs showed extensive demyelinization. Neither parent was affected, and the author felt it was due to a peripheral neuropathy of afferent nerves. He suggested that the poor nutritional state of the patients may have had an etiologic relationship.

In 1950 Fisher[22] reported two sisters at the Canadian Neurological Society. There was a negative family history; both had scoliosis and retarded early development. One had retinitis pigmentosa. Both patients had peripheral sensory loss to all modalities in all four extremities, touch being most affected, with trophic ulcerations of fingers and toes. He felt this was a familial neurovascular dystrophy, and could fit into Morvan's syndrome. We will discuss later the features which distinguish Morvan's syndrome from hereditary sensory neuropathy.

An important contribution to the understanding of the pathology of this condition was added by Denny-Brown[23] in 1951, when he reported the first necropsy of a woman suffering from hereditary perforating ulcers of the feet. This patient was a member of a family originally studied by Hicks[24] in 1922. Many members were affected, showing mild variations of the syndrome of deafness, shooting pains in the legs, peripheral sensory loss in the legs and later in the hands, greatest to pain and temperature, and with perforating ulcers of the feet. He found no evidence of significant pathology either in the spinal cord or in the anterior roots. However, there were definite changes in the dorsal root ganglia and afferent nerve trunks. There was a severe loss of ganglion cells, many of those remaining showed evidence of degeneration. He noted a marked proliferation of satellite cells about the degenerating ganglion cells, finally forming residual cellular nodules. Through these nodules there were profuse arborizations of argentophile dendrites. The peripheral nerves contributing to the ganglia showed extensive demyelinization. Alongside the residual nodules were deposits which stained lightly for amyloid. These deposits, he felt, were secondary to the ganglion cell degen-

eration and not evidence of primary amyloidosis. In support of this, he pointed out the atypical distribution of the amyloid and its absence in other body organs. He described the disease as "hereditary sensory radicular neuropathy."

Recently, two sisters aged 8 and 16 were studied by Lessard and Pouliot[25] and have since come under the care of Desrochers.[26] At ages three and six, respectively, these patients developed severe sensory loss to all modalities over the hands and feet, with diminution of some deep tendon reflexes and spontaneous loss of terminal phalanges of the fingers and toes following trophic ulcerations. There was no muscle atrophy. Desrochers has been able to secure a biopsy of the L5 dorsal root ganglion in the younger patient, and 8 cm. of the external popliteal nerve of the older sister. These have been studied by Masson,[27] and showed changes almost identical to those reported by Denny-Brown. In this case the dorsal root ganglion showed extensive loss of ganglion cells, others being in varied stages of degeneration. In their place there was proliferation of satellite cells, and formation of residual cellular nodules. There was no evidence of amyloid deposit, thus supporting Denny-Brown's original statement that these were a secondary phenomenon. There was also the proliferation of argentophile dendrites around the residual nodules. The peripheral nerve showed extensive but patchy areas of demyelinization.

As a further contribution to this syndrome, we have been able to study a family with hereditary sensory neuropathy. The pedigree was traced back through six generations, there being five cases of the classic disease, four of whom are living. In addition there were three members who showed a mild incomplete form, one of whom also showed evidence of intramedullary spinal cord disease, probably multiple sclerosis.

CASE REPORTS

Case 1. (G. P.)—A 16 year old French-Canadian boy presented himself at the Montreal Neurological Institute outpatient department complaining of a swollen left ankle of two years' duration, and was admitted on August 25, 1952 for complete study. He had three siblings who were shown to have a similar condition (case 2 [M. P.], case 3 [R. P.], and case 4 [J. M. P.]). Two other siblings, boys, were examined and considered to be normal. A fifth, a 21 year old brother, was not examined but was reported to be well and working regularly. Both parents were examined and considered normal.

The patient's mother stated that since he first started to walk at around 12 to 18 months of age, he frequently lost his balance and fell, particularly if he were in a dark room. He had always had difficulty buttoning his shirt, having to look at what he was doing in order to perform the task correctly. The patient himself did not realize anything was wrong until age nine when he cut his right index finger with a knife. Infection followed with osteomyelitis of the underlying phalanx, taking three months to heal. He lost the distal one and a half phalanges in the process. Since that time he has had frequent whitlows resulting from trauma or abrasion, followed by osteomyelitis, sloughing of tissues and bone, and loss of phalanges. Irrespective of the extent of inflammation, the infections were not painful, but he complained of painful epitrochlear and axillary lymphadenitis. He reacted severely to infections, with malaise, anorexia, fever, and generalized aches and pains over the body. Injuries and infections distal to the ankles or wrists were not painful and took a long time to heal, while those located proximally were painful and healed promptly. For example, three years ago he sustained a puncture wound of the foot which took seven months to heal. At age 13 he sustained a fracture of the right femur, which took one and a half years to heal and finally required an open reduction. Two years ago his left ankle became gradually swol-

len, inflamed, but was not tender. He could walk on it without pain, but because it became progressively larger he came to our clinic for advice.

Examination showed a pale, thin boy in no distress, who was cooperative and intelligent. The blood pressure was 115/75. He had bilateral gynecomastia. The genitalia were of normal size for his age, and there was no evidence of loss of testicular function to account for the gynecomastia. There was loss of the distal phalanges of almost all the fingers of both hands (figure 1). There were fissured, crusted lesions along the flexor creases of both hands. There was a large necrotic ulcer on the right thumb and another on the dorsum of the right hand. The toes were intact except for an ulcer under the second phalanx of the left great toe. There were long, deep, and indurated operative scars over the right anterior thigh, the site of the open reduction of the femur. The patient stood with his left foot slightly everted, and the lower part of his left ankle was considerably increased in size. The overlying skin was reddened and warmer than that over the right ankle (figure 2).

Neurologic examination revealed the cranial nerves to be intact. The pupils were equal and reacted to light and accommodation. There was no sensory loss over the face, and hearing was considered normal. There was no muscle atrophy, fasciculation, or weakness. Coordination was normal. Abdominals and all deep tendon reflexes were absent. There was no response to plantar stimulation.

Sensory examination revealed a peripheral sensory loss to all modalities in all four extremities (figure 3). The greatest loss of sensation was to cotton wool, then pain, then temperature. Least but definitely affected were position and vibration sense. The sensory loss was complete over the hands and feet, with fading borders over the shoulders and waist. There was no sphincter disturbance. Peripheral arterial pulsations were full, the skin was warm, and the patient appeared to perspire normally over all parts of the body.

Laboratory investigations included hemogram, urinalysis, blood chemistries, Wassermann, glucose tolerance curve, and liver and kidney function tests, all of which were within normal range. Cerebrospinal fluid showed normal pressure, no cells, protein 32 mg. per cent, Lange zero, Wassermann negative. There was some increase in urinary estrogens, but not in gonadotropins. The 17-ketosteroid level was low, but comparable to that seen at prepuberty. The skull, cervical, thoracic spine, and chest roentgenograms were all within normal limits. Lumbosacral spine films showed spondylolysthesis of L5 on S1. The right thigh film showed an old fracture of the upper third of the right femur. Films of the hands showed osteolytic and soft tissue changes with loss of terminal phalanges. The left ankle and foot showed fragmentation and lytic changes of bones of the tarsus and head and neck of the talus (figure 4). The terminal phalanges of the feet showed disappearance of the terminal tufts.

Case 2. (M. P.)—A nine year old girl, the sister of cases 1, 3, and 4, was admitted to the Montreal Neurological Institute on September 9, 1952, complaining of an ulcer on the sole of the right foot of two and a half years' duration. When young she also had difficulty buttoning her clothes unless she was looking, but was not as severely affected as her older brothers. She did not fall inexplicably, as did her brothers. An abnormality was first noted at age six when she was struck on the right foot. An ulcer developed which is still present. It healed for a brief time one year ago, but soon broke down again. It was noted by her physician at the time of original trauma two and a half years ago that she did not feel pain or touch in her hands or feet. The patient stated that she thought she was normal before this time, but has since become progressively worse. She has noted for the past year persistent small ulcerations occurring over the tips of the fingers of both hands. One year ago she caught her left foot on the corner of a bed, tripped and fractured her left femur. This was immediately treated by open reduction and healed well.

Physical examination revealed a very bright young girl, walking on crutches and favoring her right foot. The skin showed areas of vitiligo over the axillas, knees, and tibias. There were indurated, fissured, crusted lesions over the tips of all her fingers and over the ball of the right thumb. There was a healed indurated scar under the right first interphalangeal joint of the right great toe, and a large purulent necrotic ulcer over the lateral border of the right fifth metatarsal-phalangeal joint (figure 5). There were no phalanges missing. There was

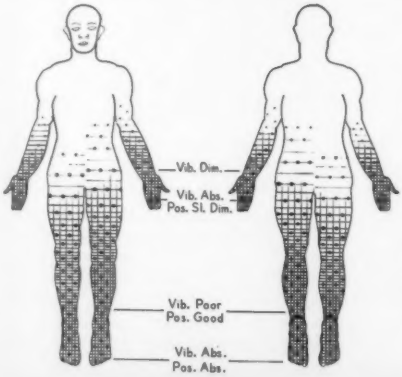
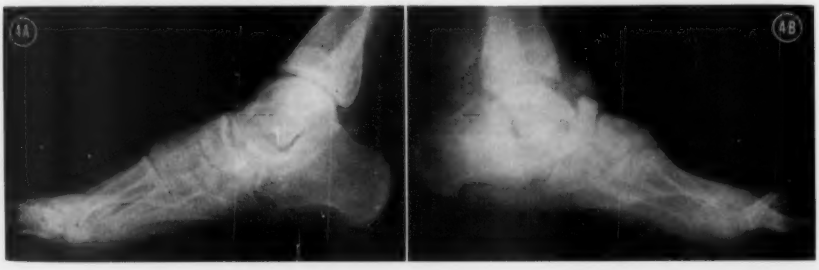


FIG. 1. *Case 1.* Photograph of the hands showing loss of distal phalanges and trophic ulcers.

FIG. 2. Photograph of the feet showing swelling of the left ankle and eversion of the foot.

FIG. 3. (*left*) Sensory chart for case 1 showing loss of sensation to all modalities over the distal aspects of the extremities. Horizontal lines represent pain loss; vertical lines represent temperature loss; dots represent touch loss.

FIG. 4. Roentgenographic studies of case 1. *A*, normal right foot and ankle. *B*, left foot and ankle showing fragmentation and lytic changes of the bones of the tarsus and head and neck of the talus.



no clinical evidence of any endocrine disturbance. There was a long indurated operative scar over the left anterior thigh. The transverse arch of the right foot was widened, swollen, slightly red, but not tender. The cranial nerves were intact. There was no muscle atrophy, fasciculation, or weakness. Coordination tests were normal. Both triceps reflexes were diminished. The remainder of the deep tendon reflexes and abdominal reflexes were absent. There was no reaction to plantar stimulation. Sensory examination demonstrated astereognosis in both hands. Position sense was slightly impaired in the fingers and toes, but present in the wrists and ankles. Vibration sense was absent in the toes and fingers and diminished

at the ankles and wrists. Touch and pinprick sensations were absent over the periphery of the four limbs, with fading borders to the shoulders and thighs. Temperature sense was greatly diminished in the toes and fingers. Arterial pulsations of hands and feet and skin temperatures were normal. She perspired normally.

Laboratory data, including urinalysis, Wassermann, hemogram, glucose tolerance curve, blood chemistries, and liver function tests, were all within normal limits. Skull, cervical, and thoracic spine films were within normal limits. Lumbosacral spine films showed bilateral spondylosis of L5. There was osteomyelitis of the right fifth metatarsal with an overlying ulcer, and an old fracture of the right navicular. There was evidence of a recent fracture of the proximal end of the first phalanx of the right great toe. The terminal tufts of the right fifth finger and the left fourth finger had disappeared. While in hospital, the right fifth toe and head of the fifth metatarsal were amputated. Good bleeding was noted at operation, and the wound healed without event. A biopsy of the right lateral femoral cutaneous nerve revealed a marked demyelinization around the axis cylinders. There was no evidence of interstitial hypertrophy in the nerve or of cellular proliferation (figure 6).

Case 3. (R. P.)—An 18 year old boy was a patient of Dr. J. C. Favreau, who kindly permitted us to examine him on September 24, 1952. Ever since this patient was able to walk, he repeatedly lost his balance and fell frequently. He always had trouble buttoning his clothes, unless he could look at what he was doing. At the age of seven he broke a bone in his left foot without any associated pain. Eight months later he developed aching pains in both feet which disappeared after an operation in which his arches were stabilized. This pain was remembered as being of the burning and squeezing type. The patient has had persistent painless ulcerations of the fingers and toes, and at the age of 16 his left leg was amputated below the knee because of trophic ulcerations and osteomyelitis of the left foot and ankle. He felt the disease was progressive until the last two years, when the advance definitely slowed and the infections became less frequent. In 1951 he was operated on for appendicitis without any particular difficulty.

Physical examination revealed an intelligent and cooperative patient. All the distal phalanges of both hands were missing, and the stumps were ulcerated; the left leg was amputated below the knee. There was a warm soft tissue swelling at the end of the amputated stump. The cranial nerves were intact. Motor power and coordination tests were normal. Superficial and deep tendon reflexes were all absent. Sensory examination demonstrated diminished position sense in both fifth fingers and absent position sense in the toes of the right foot. Vibration sense was lost over the fingers of both hands, over the right toes, and the left stump, and diminished over the right tibial surface. Touch was lost over both legs with fading borders at the midthigh level, and absent over the hands and forearms, with fading borders above the elbow. Pain was lost over both hands and forearms, fading just below the elbows, and lost in both legs up to the knees. Temperature was felt first over the lower forearms and below the knees, being absent below that.

Summary: These three siblings, therefore, show the syndrome of an illness with an onset very early in life, if not indeed present at birth, characterized by difficulty in gait, progressive peripheral sensory loss to all modalities, and trophic ulcers over the hands and feet. As far as one could tell, there was no evidence of muscle atrophy or weakness in the deformed extremities.

Case 4. (J. M. P.) This patient, a 12 year old boy, was examined on October 23, 1952. He had been well, with no complaints and no trouble with walking or buttoning his clothes.

The cranial nerves and motor system were intact. Both biceps reflexes were markedly diminished, but the remainder of the reflexes were normal. Pain and temperature sensation was diminished over the hands and feet, but was appreciated over the shoulders and thighs. Position and vibration sense were intact. Cotton wool sensation was diminished over the hands and forearms and improved as one approached the shoulders. There was slight loss to cotton wool over the lower legs to the thighs.

This sibling, who had no complaints, showed mild peripheral sensory loss to touch, pain, and temperature, with diminution of both biceps reflexes.

Case 5. (S. G.)—This patient, aged 80, was a patient of Dr. A. Beaudoin, and was examined on October 23, 1952. He was the nephew

FIG. 5. *Case 2.* Photograph of the feet showing a large necrotic ulcer over the lateral border of the right fifth metatarsal-phalangeal joint.

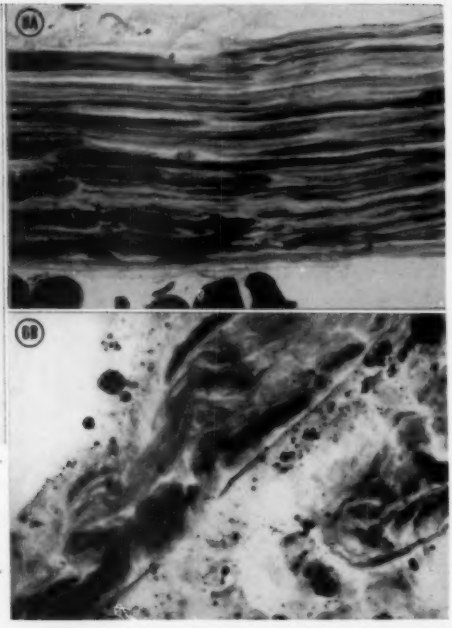


FIG. 6. *A.* Photomicrograph of a normal lateral femoral cutaneous nerve taken from an adult patient without neurologic complaints. *B.* The right lateral femoral cutaneous nerve of case 2 with marked demyelinization present. Osmic acid stain.

of the paternal great grandmother of cases 1 to 4. He had had loss of sensation in the hands and feet as long as he could remember. As a child he thought it was normal to be like that. While a young boy he developed trophic ulcers of the fingers and toes, and over the years he spontaneously lost the distal half of his right foot. He felt that the disease has been progressive all his life, and he still had recurrent ulcers over his feet. He felt abdominal pain and hunger. The patient had an elder brother with exactly the same complaints who died at the age of 15 following amputation of an infected toe. This patient remembers his brother well, and he feels that he is suffering from an identical illness.

On physical examination he presented as an elderly white male, alert, intelligent, and cooperative. The tips of the second and third fingers of the right hand were shortened and scarred. There was a right midtarsal amputation, and the stump had two ulcers on the plantar surface. The distal phalanges of the toes of the left foot were missing. The cranial nerves were intact. He had good strength and coordination. The right biceps and both triceps reflexes were markedly diminished. The remainder of the superficial and deep tendon reflexes were absent. There was pain loss to the mid-arm level with fading borders to the shoulders, and over the legs with fading borders up to the costal margins as high as T4. There was temperature loss to the elbows and knees with fading borders. There was absent touch over the arms to the shoulders and over the legs and body up to T4 with fading borders. Position sense was absent in the fingers and toes. Position sense was absent up to the iliac crest and up to the shoulders, but was felt over the xiphoid process and clavicle.

This, then, is a distant relative, at least two generations removed from cases 1 to 4, with an identical syndrome. In all probability, his brother suffered from the same disease. The fact that this patient was 80 would indicate that with proper care, the disease does not necessarily have a poor prognosis.

Case 6. (R. D.)—A 38 year old man was of the same generation as cases 1 to 4 and their first cousin. He was well except between the ages of 18 to 20 when, working as a laborer, he developed frequent infections of the fingers of both hands. These would quickly get out of control, with lymphadenitis and swelling of his arms and axillas. The lymph nodes were only moderately painful, but had to be incised and drained. He has since had no further trouble, and has worked regularly as a baker and a store clerk.

There was an old deep scar over the tip of the left third finger from a previous infection. The cranial nerves were intact. The motor system was intact. Reflexes were normal. Position and vibration sense were normal. Touch was diminished over the dorsum of both hands. Pain sense was intact. There was definitely diminished sensation to heat and cold over the hands and forearms, over the feet and shins, more marked distally, with fading borders, becoming normal over the shoulders and thighs.

This is a first cousin of the affected siblings, with a brief period of two years when infections flourished. He is now well, but still shows very definite signs of peripheral sensory loss.

Case 7. (J. N. G.)—This man, aged 48, a first cousin of the father of cases 1 to 4, was examined through the courtesy of Dr. Louis D'Esopo. The patient gave a history of staggering gait since age 25, inability to perform fine movements with the right hand since age 35, and weakness of the right arm and leg over the subsequent years. He was studied at the New York Neurological Institute in 1941, where a diagnosis of multiple sclerosis was made. He was seen at the Montreal Neurological Institute in 1945, where bilateral pyramidal tract signs were noted, more marked on the right side. There were also many indurated scars present over both tibias. Investigations, including pneumoencephalogram, added little positive information. He was seen on December 11, 1952, and further history was obtained that between ages 28 to 30 he had suffered recurrent boils over his neck, arms, and legs, leaving him with residual scars. He also stated that he had had a sister who died at age 30 of a neurologic illness diagnosed as multiple sclerosis.

On examination he showed horizontal nystagmus on gaze to either side, more marked in the abducting eye, and spasticity of all four extremities, more marked in the hemiparetic right arm and leg. The deep tendon reflexes were bilaterally hyperactive, with bilateral extensor plantar responses. Only the upper abdominal reflexes were obtained. Sensory examination revealed diminished sensation to pain, temperature, and vibration over the fingers and toes of all limbs. There were many scars over the anterior tibial surfaces.

In this case, the diagnosis of a myelopathy, probably multiple sclerosis, seems justified. The two year period of skin infections and the mild peripheral sensory loss is similar to case 6, but need not be due to primary peripheral neuropathy in this instance.

FAMILY HISTORY

We have thus been able to review six generations in this French-Canadian family, numbering at least 144 people. The information was obtained by interviews with members of each generation, the data for generations 1 and 2 being obtained from several living members of generation 3. The members of this family were keen observers, extremely cooperative, and interested in this study. Many of them had kept personal written accounts of preceding family histories, and were able to furnish the names, age at death, and cause of death for many members.

Only representative families with a large number of children were included in the family chart in order to demonstrate the fact that no other known case had occurred in that generation (figure 7). Neonatal deaths have been omitted from the chart. Almost every married member has a large number of children, and relatives as close as aunts, uncles, and first cousins were able to give information as to their state of health.

It will be seen that the classic, complete, and severe form of this syndrome is represented by cases 1, 2, and 3, and by case 5 and his dead brother. That

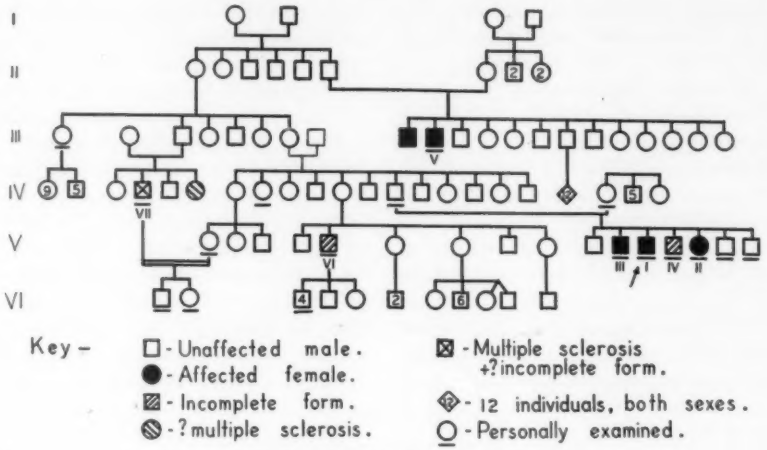


FIG. 7. Family history chart for cases described in this study.

case 5's older brother had the same disease would seem unquestionable from the information received. In a family as closely knit as this, it seems unlikely that a similar condition would have passed unnoticed. These cases have occurred in the third and fifth generations, with latency in transmission over at least two generations. The parents of cases 1 to 4 have been examined and found to be normal.

Cases 4, 6, and 7 all showed only mild peripheral sensory loss, and represent, we believe, an abortive or arrested form of the disease. It is possible that case 4 is showing the first manifestations of the complete form as represented by his siblings. Cases 6 and 7 have passed through a brief term of infection and ulcerations with a subsequent period of stabilization and improvement.

The hereditary pattern seems best explained by transmission of a dominant gene with reduced penetrance and variable expressivity. A review of the family histories of Thévenard and Denny-Brown showed the transmission to be of a dominant type.*

In case 7, it seems most likely that the patient is suffering from a rather chronic progressive form of a demyelinating disease, probably multiple sclerosis. He was, in addition, discovered to have mild peripheral sensory loss and a history of a period of easy infectivity. We have only his information and that of his wife and relatives that one sister died of a similar disease diagnosed as multiple sclerosis.

DISCUSSION

The possibility that these patients could have had generalized amyloidosis was considered. In this condition it has been shown that both the dorsal root ganglia and peripheral nerves may be affected.[28] In our cases, however, the family history, duration of the disease, and the lack of systemic disorders were not compatible with that diagnosis.

*Dr. F. Clarke Fraser of the department of genetics, McGill University, served as consultant.

Hypertrophic interstitial polyneuritis seemed improbable from the clinical findings. The peripheral nerves were not hypertrophied, there was no nystagmus, tremor, or muscular atrophy, and the biopsy of a cutaneous nerve in case 2 did not show any evidence of connective tissue hypertrophy or nuclear proliferation.

In the past, the diagnosis of Morvan's disease has been made in a number of cases which, as Parks and Staples have pointed out, are more properly classified as sensory neuropathies. It is, therefore, pertinent to consider the long neglected subject of Morvan's disease and to determine what relation, if any, it may have to sensory neuropathies.

H. Morvan, of Lannilis, France, published a series of papers from 1883 to 1889[29–33] on a disease which he named, "La parésie analgésique a panaris des extrémités supérieures, ou parésoanalgésie des extrémités." The protocols of 19 cases were presented over the six year period, plus a brief account of another case seen many years before 1883. There were six females; most of the men were farmers, some were fishermen. Most of the patients, but not all, were from Brittany. The usual age of onset was from 20 to 50 years, the youngest at age 15, the oldest at age 52. The first two papers described the clinical course as beginning with neuralgic pains in the upper limbs, followed by weakness and varying degrees of atrophy in the hands and forearms. Later, loss of touch, pain, and temperature sensation in peripheral distribution occurred, first on one side, then the other, involving the hand, forearm, and arm, and occasionally the face, neck, and chest. Finally there was the appearance of painless whitlows. Charcot,[34] in 1890, noted that the weakness and sensory loss could precede the pains, and Morvan[33] admitted to "cas frustes" where the whitlows were painful and where there was no weakness or sensory loss. The course was one of very slow progression, usually ten to 20 years. One case had a 20 year interval between the appearance of ulcers on one hand and the other. In case 12 the sensory loss extended over the left face, neck, arm, and hand; in case 13 it involved the upper chest. In only two cases, 7 and 16, were the legs involved, one leg in each patient, with sensory loss, weakness, and ulcers. He noted an absent radial reflex in case 16 in the affected arm but none had lost their knee jerks, even those with leg involvement. Morvan[31] described associated arthropathies in three cases and scoliosis in six.[32] Broca[35] also noted scoliosis, and Prouff[36] noted arthropathies.

Although Morvan felt the cause to be an intramedullary cervical cord lesion, he tried to draw a distinction between his cases and syringomyelia. He stated that trophic disorders and touch loss did not occur consistently in the latter disease, as it did in his cases. He was in favor of another type of "atrophic disease."

As far as we can detect, only two complete autopsies have been reported, the first in 1889 by Prouff, Gombault, and Reboul;[37] the second in 1890 by Joffroy and Achard.[38] The first was a 56 year old woman with a negative family history who developed scoliosis and ulcers of the right fingers at age 12 and ulcerations of the left hand at age 40. She had had pain in her arms from time to time. On examination she had an arthropathy of the right shoulder, coldness and cyanosis of both hands with loss of terminal phalanges, and great atrophy of all the small muscles of the left hand.

There was loss of pain, temperature, and position sense in both arms. The patient succumbed to a septicemia. At autopsy the brain was not remarkable, but the peripheral nerves in the upper limbs showed severe demyelination, complete in the hand, patchy at the shoulders. The nerves were considerably hypertrophied with dense interfascicular connective tissue. The sciatic and internal popliteal nerves were normal on cross-section. The dorsal root ganglia showed numerous and normal ganglion cells with normal connective tissue. The arteries in the pia and about the peripheral nerves showed profound changes, with thickened walls, diminished lumen size, occasionally occluding the vessels, with hyaline degeneration of their walls. Gombault (who presented the findings) severely traumatized the spinal cord during its removal. In the cervical region the central canal was voluminous, the central gray matter had more connective tissue and less nerve fibers than usual. In this region there were many areas of cavitation extending radially into the posterior horns. The authors felt that this could have been due to the severe manipulations of the cord during its removal, and noted that the cavities occurred where the hammer blows had fallen, that the borders of the cavity were fissured radially and irregularly with no limiting membrane or surrounding gliosis, and that the contents of the cavity was detritus composed of connective tissue and nerve tubes. He did not emphasize the changes which were present in the nerves of the upper limbs.

The second autopsy, by Joffroy and Achard, was that of a 75 year old woman whose family history was negative. She had a two months' illness at age 30, with rather abrupt onset of ulcers, pain, and loss of phalanges of both hands. These soon healed, and from age 30 until age 36, when she was seen at the Salpetrière, she had no further lesions and had worked as a domestic during that time. On examination she showed thickened skin and loss of terminal phalanges of both hands, with loss of position sense in both hands, and loss of touch, pain, and temperature sensation over both arms, with fading borders at the shoulders. There was no gross muscle atrophy. She died at age 75 of bronchopneumonia. At autopsy the brain and general organ examination were not remarkable. The arteries along the peripheral nerves in the arms and in the pia were thickened and often occluded. There was some muscle atrophy in the small muscles of the left hand, not considered remarkable on clinical examination. In all the nerves of the arms there was demyelination, most marked peripherally, with an increase in the interfascicular connective tissue. In addition, in the cutaneous nerves of the fingers, there were small globules, like psammoma bodies, colored pink with carmine, bypassed by myelin sheaths, and not traversed by them. Also, on the internal lamellar sheath he found a fibrous nodule containing elongated nuclei. In the spinal cord, extending from C1 to T4, was a typical syringomyelic cavity, while situated centrally, it extended into both posterior horns throughout its whole length, destroying them as well as both dorsal columns. In addition, the spinocerebellar tracts were sclerosed. No mention was made of the dorsal root ganglia. Joffroy concluded that the primary pathology in Morvan's syndrome was located in the central gray matter, but did not feel that it had to be syrin-

gomyelic cavitation in all cases. He also stated that this lesion was insufficient to account for the complete clinical picture, noting the existence of a peripheral neuropathy in Gombault's and his cases, as well as in the nerves of a finger amputated from a third case reported by Monod and Reboul in 1888.[39]

However, Charcot[40] reviewed these findings in 1891 and felt that Morvan's syndrome should be included in the syringomyelic group. Up to the present date, this seems to be where the question has been left. It did not prevent Dejerine[41] from criticizing this decision because, he stated, Morvan's cases were too numerous to be due to syringomyelia and a central lesion could not explain the peripheral sensory loss. He considered that these cases more properly belonged to the peripheral neuropathies. Cruchet and Delmas-Marsalet,[42] in commenting on the controversy, quoted from a letter which Prouff wrote to Achard around 1892. Prouff stated that five autopsies had been done up to that time, four yielded syringomyelic cavities, and one (Gombault's) was doubtful.

The apparent lack of recorded autopsy studies makes it harder to form a final decision as to the true pathology of Morvan's syndrome. That it differs from hereditary sensory neuropathy is evident. In Morvan's syndrome, the predominant affection of the upper limbs, the lack of hereditary pattern, the muscular atrophy, the relative preservation of the deep tendon reflexes, the patchy and occasional forequarter sensory loss, all point to a separate entity. The lack of pathology in the dorsal root ganglia in the reported autopsies supports this conclusion. We believe that Morvan's disease is a syndrome, as described above, which is caused by an intramedullary cervical spinal cord lesion. The most frequently seen process liable to produce the typical clinical picture and course is syringomyelia.

In his report on hereditary sensory neuropathy, Denny-Brown[23] reviewed the differential diagnostic possibilities, the mechanism of trophic ulcer formation, and compared the pathology of different processes which could give rise to similar clinical pictures. He commented on the fact that the greater loss to pain and temperature than to touch in his case could be explained on selective degeneration of fibers in the dorsal root ganglia, the unmyelinated and small myelinated fibers being most affected. This is of importance due to the usual association of dissociated sensory loss with intramedullary pathology.

He related the entity of hereditary sensory neuropathy, being a disease of the dorsal root ganglia, to Charcot-Marie-Tooth peroneal muscular atrophy. The latter represents the motor form of degenerative disease, while the former represents the sensory. In betwen, he would put those cases of peroneal muscular atrophy which also show severe sensory change and trophic disorders, as he reported with England.[43] We have been struck by the definite symmetrical and peripheral type of sensory loss observed in these patients, even in early cases of the disease, as represented by case 4. Some cases have been observed early in their development by Denny-Brown, who stated[44] that the sensory loss is usually along the lateral border of the calves. One can only suggest that in addition to the primary ganglion pathology there is another factor, the nerve length. The longer the fiber, the more susceptible it is to degeneration. We

have recently seen a boy age 12 suffering from hereditary sensory neuropathy, who came from a family unrelated to our cases. He had sensory loss not only in the hands and feet but also on the anterior abdominal wall. There was a gradual increase in sensitivity to pain and temperature as one proceeded from the midline in front around the trunk to the back.

This condition, we feel, is probably due to some metabolic error, transmitted by a dominant gene from generation to generation. The metabolic error could be either a defective enzyme system which alters the intermediary metabolism of available food elements with the accumulation of some toxic product, or a defect of peripheral nerve enzymes in the utilization of normal food sources. In either case dorsal root neurons with long axons seem to be particularly susceptible. It is of great interest, in this respect, to review the two cases of sensory neuropathy which developed in association with bronchogenic carcinoma, reported by Denny-Brown.[45] The typical residual cellular nodules were again found in the dorsal root ganglia, and he postulated some product of the carcinoma metabolism which might interfere with normal ganglion function. It may be noted that in one case there were metastases around the cardiac portion of the stomach, and in the second case there was a megacolon. Denny-Brown[23] also commented on the ataxia produced in swine by pantothenic acid deficient diet reported by Wintrobe and co-workers.[46,47] In these experiments the pathologic findings in the dorsal root ganglia were also one of loss of ganglion cells with residual cellular nodule formation.

A further case of sensory neuropathy has been reported by Dodgson and Hoffman,[48] which developed in association with an esophageal carcinoma. Sensory loss and absent tendon reflexes developed in the legs. Only one dorsal root ganglia was examined, and did not reveal the typical changes already described. Perhaps the common feature in both groups is some interference with gastrointestinal function.

There is no question that the patients presented here fall into the group of hereditary diseases of the nervous system, of which the sensory neuropathies form a distinct group. One need hardly mention the need for further studies of the metabolism of normal and abnormal nerves. The information thus obtained can be directed toward understanding the fundamental biochemical derangements, and to the planning of an effective therapeutic approach in the field of peripheral neuropathies.

SUMMARY

1. Hereditary sensory neuropathy is a condition transmitted by a dominant gene, causing a severe peripheral sensory loss, loss of deep reflexes, and severe trophic disorders of all four extremities.

2. The historic background of this condition is reviewed.

3. A family history in which this condition occurred is presented. The pedigree was traced through six generations. There were five cases of the classic disease, four of whom were living. Three other members showed an incomplete form.

4. The relationship to Morvan's disease is discussed.

5. The primary pathologic lesion is in the posterior root ganglion. However, another important factor seems to be the length of the nerve from its ganglion.

It is felt that there must be a metabolic error due either to a defective enzyme system which alters the intermediary metabolism of available food elements, with the accumulation of some toxic product, or a defect of peripheral nerve enzymes in the utilization of normal food sources.

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IT HAS BEEN SEEN in the preceding history of the disease, and in the accompanying cases, that certain affections, the tremulous agitations, and the almost invincible propensity to run, when wishing only to walk, each of which has been considered by nosologists as distinct diseases, appear to be pathognomonic symptoms of this malady.

1. *Involuntary tremulous motion, with lessened voluntary muscular power, in parts, not in action, and even supported.* It is necessary that the peculiar nature of this tremulous motion should be ascertained, as well for the sake of giving to it its proper designation, as for assisting in forming probably conjectures, as to the nature of the malady, which it helps to characterise.

The separation of palpitation of the limbs (*palmos* of Galen, *tremor coactus* of de la Boe) from tremor, is the more necessary to be insisted on, since the distinction may assist in leading to a knowledge of the seat of the disease. It is also necessary to bear in mind, that this affection is distinguishable from tremor, by the agitation, in the former, occurring whilst the affected part is supported and unemployed, and being even checked by the adoption of voluntary motion; whilst in the latter, the tremor is induced immediately on bringing the parts into action. Thus an artist, afflicted with the malady here treated of, whilst his hand and arm is palpitating strongly, will seize his pencil, and the motions will be suspended, allowing him to use it for a short period; but in tremor, if the hand be quite free from the affection, should the pen or pencil be taken up, the trembling immediately commences.

James Parkinson in *An Essay on the Shaking Palsy*, published in 1817.

Diagnostic Localizing Value of Muscle Atrophy in Parietal Lobe Lesions

Alex Silverstein, M.D.

MUSCULAR ATROPHY is neither a new nor an infrequent finding in cerebral lesions. It has been the object of numerous studies by many outstanding neurologists of the past century; yet its prevalence and clinical significance have not been properly evaluated.

The author's interest in this subject was aroused in 1927 when observing a patient with meningioma of the parietal lobe. This patient exhibited an intense unilateral hemiatrophy which, together with other localizing signs of the parietal syndrome, disappeared following extirpation of the tumor. Subsequent to this initial experience, careful and systematic examination of the skin and muscles in patients with suspected brain lesions has disclosed that amyotrophy is a frequent finding in parietal lesions. Its importance as a localizing sign of parietal disease has been emphasized in several earlier reports.[1] Attention has been directed to its diagnostic value in patients exhibiting clouded sensorium and psychotic or toxic states when a satisfactory neurologic examination is impossible.

While current textbooks and literature scarcely mention the subject of cerebral amyotrophy, a recent French textbook on neurology[2] and a number of investigators reporting chiefly in the French journals have corroborated the diagnostic value of atrophy as a localizing sign in parietal lesions.

CASE MATERIAL

This presentation is based on an analysis of atrophy in three groups of cases divided according to etiology.

GROUP 1 consisted of ten cases of tumors of the parietal lobe showing the triad of atrophy, flaccidity, and cortical sensory loss. In all these cases atrophy was an important clinical feature.

GROUP 2 consisted of 30 cases of infantile cerebral lesions, chiefly porencephaly, with hemiplegia, atrophy, sensory loss, and convulsive seizures as the outstanding clinical characteristics. Illustrative cases are recorded to demonstrate that variations in the involvement

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of atrophy and decrease in growth may depend upon the position of the brain lesion.

GROUP 3 comprised 50 cases of hemiplegia divided into two subgroups. In the first subgroup were 28 cases with atrophy in the paralyzed extremities which was associated with hypotonia and sensory loss, especially astereognosis. Illustrative cases of this subgroup are presented. They include two cases due to complete occlusion of the middle cerebral artery as demonstrated by arteriography. The second subgroup consisted of 22 cases without atrophy, who had no sensory defect and paralysis usually of spastic type.

REVIEW OF LITERATURE

Since comprehensive surveys of this subject have been made by Chatin[3] in 1900 in the French literature, by Steinert[4] in 1906 in the German literature, and by Winkelman and Silverstein,[5,6] only a cursory reference will be made to earlier contributions.

While some of the earlier writers considered atrophy in hemiplegia to be uncommon, others like Gilles de la Tourette,[7] Marinesco,[8] and Darkschewitch[9] insisted that it was a frequent symptom. Charcot,[10] who made the first important study, believed that atrophy was due to a descending sclerosis of the pyramidal tract, with secondary involvement of the anterior horn cells. Although Babinski showed later that atrophy could occur without a lesion in the cord or peripheral neuron, the anterior horn cell theory has had many followers. Weisenberg,[11] in a study of 160 cases of hemiplegia, found that more than half showed wasting and sensory changes were found in the majority of these cases. Chatin[3] reported 19 cases of hemiplegia which were divided into two groups: 11 cases with atrophy had associated sensory loss, and eight cases without atrophy had no sensory defect. His findings correspond with those reported by many other investigators.

There are a number of important papers on amyotrophy associated with traumatic injuries of the parietal lobe. Patella[12] recorded a case of fracture of the parietal bone which produced contralateral atrophy with hemiparesis. Rhein[13] reported the case of a patient with a gunshot wound of the right parietal motor region with contralateral hemiparesis, astereognosis, and atrophy. A most significant contribution was made by Guthrie,[14] based on a study of a number of cases of head injuries sustained in World War I. He found that all cases of postcentral injuries were associated with contralateral muscle atrophy, hypotonia, and sensory disturbances. He particularly stressed skin changes, the "ladylike" hand, and significantly, the absence of motor disturbance. Head[15] also described similar skin and muscle changes in injury to the parietal lobe.

Particularly important is the recent contribution of Penfield and Robertson,[16] who demonstrated that cortical lesions occurring before three years of age, when limited to the postcentral gyrus, are regularly associated with a contralateral decrease in growth with moderate muscular atrophy, whereas similar lesions in the frontal, occipital, and temporal lobes of the cerebral cortex are not associated with such changes. These authors also presented evidence that trophic function is closely related to sensory representation in the cortex. In several of their patients impaired growth was limited to the hand and even to one

metatarsal bone due to a focal lesion in a corresponding specific area in the postcentral gyrus.

That congenital malformations in the parietal lobe can cause trophic changes in the contralateral extremities was demonstrated by Gowers[17] in a case of failure in prenatal development of one hand which was associated with atrophy in the corresponding contralateral postcentral gyrus. Bastian and Horsley[18] reported a similar case.

Numerous reports of tumors in the parietal lobe mention unilateral atrophy as a prominent sign. In the case reported by Packard,[19] atrophy was described "precisely that of an advanced case of idiopathic muscular atrophy." Following study of a case of unilateral atrophy due to a tumor in the superior parietal lobe, Mills[20] concluded that "the cerebral trophic centers are probably not to be sought for in the motor region of the cortex, as has been suggested by some observers, but in the limbic and parietal lobes." Prince[21] was one of the first to emphasize that advanced muscular atrophy simulating spinal cord disease can occur in the early phase of brain tumor with relatively mild motor impairment. Christiansen[22] pointed out that amyotrophy is of greater diagnostic importance than is usually credited. In a study of 21 cases of brain tumor, seven out of nine cases with a parietal position exhibited amyotrophy. He stressed muscle wasting as an early sign and may precede motor involvement. He believed that jacksonian seizures play a role in the mechanism of atrophy since the wasting is more pronounced in muscle segments where the localized convulsions originate.

The more recent foreign literature corroborates the author's earlier reports emphasizing the diagnostic value of muscle atrophy as a localizing sign of parietal disease. Guillain, Petit-Dutaillis, and Rouques[23] in 1932 presented a case of a cystic glioma of the parietal lobe which was associated with muscular atrophy in the contralateral extremity. The authors were impressed with amyotrophy as an important localizing sign of parietal disease. Barré, in a discussion of this presentation, also stressed the diagnostic value of atrophy and referred to the case published in 1925[24] under the title of "Unilateral Amyotrophic Lateral Sclerosis." Van Bogaert[25] in 1933 reported on two cases of tumor in the parietal lobe in which the wasting was early, intense, and in each instance preceded the appearance of motor dysfunction. The first case was erroneously diagnosed and treated as syringomyelia. Van Bogaert was particularly impressed with the significance of amyotrophy as an important diagnostic sign of parietal involvement. Pitha[26] reported four cases of parietal lesions, three gliomatous and the fourth a tuberculoma. Especially interesting was his report on the third case, a precocious atrophy of the face and half of the tongue in addition to focal facial seizures. While Pitha admitted the frequency of muscle atrophy as a sign of parietal lesions, he attributed the mechanism to an implication of the pyramidal tract, either by compression of the motor pathways or interference with the association fibers connecting the frontal and parietal areas. Delmas-Marsalet[27] stressed the relationship of sensory loss to atrophy; in his two cases atrophy progressed proportionately to the intensity of sensory loss and improved as the sensation returned. In the case of frontoparietal glioma reported by Roger, Arnaud, Pousines, and Paillas,[28] atrophy of the

upper limb was associated with fibrillations, pyramidal tract signs, sensory loss, and convulsive seizures. Schwob,[29] in his thesis on the parietal lobe, discussed the diagnostic value of atrophy as a sign of parietal lobe dysfunction. Austregesilo[30] described a case of parietal lobe tumor with severe wasting of the upper limb. David, Hecaen, and Sauguet[31] reported two cases. The first resembled the Aran-Duchenne type of wasting, which occurred early with well-marked vasomotor findings of cyanosis, sweating, and oscillometric changes. The second case showed intense atrophy which occurred early with mild pyramidal tract signs. In both instances sensory changes, including astereognosis, were present. The authors corroborated the localizing value of atrophy in parietal disease and stressed the superficial position of the lesion. They urged systematic, careful examination for atrophy in patients with cerebral lesions. Amyot,[32] reporting on a case of infiltrating glioma operated upon by Penfield, concluded that while the mechanism of amyotrophy remained obscure, it was a valuable diagnostic sign in parietal lesions. Fragnito,[33] studying a case of cerebral tumor from the onset of initial symptoms, concluded from the clinical picture indicating extension of the tumor from the motor cortex to the parietal area that atrophy is a significant parietal lobe sign since it occurred promptly together with the other signs of parietal syndrome.

PRESENTATION OF CASES

GROUP 1 consisted of ten cases of tumors of the parietal lobe showing the triad of atrophy, flaccidity, and cortical sensory loss. In all these cases atrophy was an important feature in establishing the diagnosis (table 1).

Case 1.—Parasagittal meningioma with early symptoms of coldness and atrophy of the leg, diagnosed as poliomyelitis. Complete disappearance of atrophy following removal of tumor.

A 31 year old white woman complained of coldness, sweating, and wasting of the right lower extremity, apparently following an attack of grippe in September 1940.

Examination: Five months later examination revealed motor impairment of the right lower extremity with weakness of the adductors, external rotators of the hip, flexors of the leg, and paralysis of the extensors of the foot and toes; also left-sided foot drop with paralysis of the extensors and flexors of the toes. The striking feature was the wasting of the right lower limb which was 1½ cm. less in circumference in the thigh and 2½ cm. less at the level of the calf than the left limb. The skin of the right foot and leg was smooth and glossy. A presumptive diagnosis of residual poliomyelitis was made.

Two weeks after this examination, focal motor seizures developed with progressive increase in weakness of the right leg. Reexamination eight months later (13 months from the onset) revealed a spastic paralysis of the right lower extremity, with increased patellar reflexes, ankle clonus, and Babinski sign. In the left foot the previous loss of flexion and extension of the toes was still evident, and atrophy of the muscles in the right lower limb was more pronounced. The right thigh measured 35 cm., the left 38½ cm.; right calf 30 cm., left 33 cm.; right ankle 19 cm., left 20½ cm.

The patient was admitted to Temple University Hospital on November 5, 1941 with a diagnosis of parasagittal meningioma chiefly affecting the left paracentral lobe. Five days later a large parasagittal meningioma was removed which required ligation of the rolandic vein.

Postoperative course: There was right-sided flaccid hemiplegia, marked sensory loss, and increase in wasting of the muscles for about six days, followed by complete disappearance of these signs. The only residual finding, six months later, was a mild weakness of flexion and extension of the toes of the right foot.

Comment: The clinical picture in this case of atrophy and irregular paralysis of muscle groups in both lower extremities was sufficiently striking to warrant a diagnosis of poliomyelitis. However, progression of the atrophy with focal

TABLE 1

GROUP 1—TUMORS OF THE PARIETAL LOBE SHOWING THE TRIAD OF ATROPHY, FLACCIDITY, AND CORTICAL SENSORY LOSS. 10 ILLUSTRATIVE CASES

Case No.	*Sex*	*Age*	*Clinical Picture*	*Choked Disk*	*Atrophy*	*Operation*	*Course*
1	F	31	Coldness, sweating, atrophy right leg, irregular paralysis of both legs	No	Right leg	Removal of parasagittal meningioma	Disappearance of atrophy with other focal signs
2	M	30	Convulsions, early atrophy followed by hemiparesis, sensory loss	No	Right arm, less in leg	Removal of glioblastoma of parietal lobe	Improvement in motor and sensory signs—progressive increase in atrophy
3	M	47	Left-sided atrophy, flaccidity, sensory loss following removal of glioma in right temporal lobe	No	Left arm, less in leg	Removal of recurrent glioma of parietal lobe	Improvement in motor and sensory signs, increase in wasting
4	F	63	Nervousness, bromide intoxication, early atrophy diagnostic	No	Left arm		Necropsy, glioma in subcortical parietal lobe
5	M	69	Aphasia, symptoms of cerebral and cardiovascular disease. Progressive atrophy diagnostic	No	Right arm	Removal of astrocytoma of parietal lobe	Death—no necropsy
6	M	44	Removal of glioma from left superior temporal lobe, recurrence with atrophy, hemiparesis, sensory loss	No	Right arm, less in leg	Removal of recurrent glioma of parietal lobe	Improvement in motor and sensory signs, increase in wasting
7	M	36	Flaccidity, sensory loss, atrophy, superimposed upon ulnar nerve syndrome	Not until late	Right hemiatrophy including face		Necropsy, metastatic lesions in right 7th and 8th cervical vertebras and left parietal lobe
8	M	38	Labelled "schizophrenic." Atrophy diagnostic in detecting signs of a focal lesion	No	Left arm and leg	Removal of astrocytoma of parietal lobe	Necropsy, metastatic lesions in upper cervical and contralateral temporoparietal lobes
9	F	44	Focal seizures, progressive weakness, atrophy in left leg	Yes	Left leg, less in arm	Removal of hypernephroma of parietal lobe	Temporary improvement in clinical signs
10	M	46	Left-sided jacksonian seizures, atrophy diagnostic localizing sign. Two negative arteriograms and air encephalograms	No	Left arm and thigh	Removal of astrocytoma of parietal lobe	Improvement in motor power, progressive increase in wasting

seizures strongly indicated a lesion in the contralateral paracentral lobe. The postoperative transient occurrence of flaccid paralysis, muscle wasting, and sensory loss is a triad frequently observed following surgical injury to the parietal region.

Case 2.—Glioma of left parietal lobe in a patient treated for epilepsy. Atrophy of diagnostic significance in establishing correct diagnosis.

A 30 year old weaver was admitted to Northeastern Hospital on January 5, 1939 with a history of right-sided jacksonian and major seizures during a two and one-half year period. At first the seizures occurred once every three weeks, gradually increasing to one to three times daily. Following one of his attacks, weakness of the right arm and leg developed. In 1938 he had been studied on two occasions by the neurologic service of a leading hospital with apparently negative results.

Examination: There was a mild right hemiparesis with skin changes, "ladylike" hand, atrophy of the right upper limb (figure 1), and mild cortical sensory defect. There were no objective or subjective symptoms of increased intracranial pressure.

Operation revealed a glioblastoma occupying almost the entire parietal lobe. The tumor was removed by suction.

Postoperative course: Motor power improved so that he was able to raise the right arm above

FIG. 1. *Case 2.* Right-sided hemiatrophy in a patient with a glioma of the left parietal lobe.

his head and flex his elbow. However, the skin changes and wasting of the muscles progressively increased. The skin was described at this time as "like that of a baby."

Comment: This patient was studied and treated as a case of epilepsy in a recognized neurologic clinic until atrophy and skin changes led to restudy of the patient which established the correct diagnosis. As in most of our cases, the usual signs of increased intracranial pressure were absent until late in the course of the disease.

Case 3.—Recurrence of a right temporal glioblastoma with extension into the parietal lobe, producing the characteristic triad of atrophy, flaccid paralysis, and sensory loss.

A 47 year old coal miner was admitted to Temple University Hospital on June 8, 1943 with a history of a glioblastoma of the right temporal lobe removed eight months previously. The patient said that previous headaches and visual disturbance had improved following the operation, but recurred two weeks prior to his second admission.

Examination: There was a left homonymous hemianopsia, weakness of the left arm and leg, cortical sensory defect, and moderate atrophy of the muscles of the left leg and arm.

Operation: A glioblastoma in the parietal lobe extending upward from the temporal lobe was removed, leaving a cavity equivalent to accommodate 3½ oz. of fluid.

Postoperative course: There was rapid development in the clinical picture, with progressive left flaccid hemiplegia, depression of deep reflexes, marked sensory loss including astereognosis, skin pale and smooth, and profound wasting of the muscles of the entire left side of the body, chiefly affecting the upper limb (figure 2).

Comment: When the lesion was limited to the right temporal lobe there was no atrophy. With recurrence of the tumor and invasion of the parietal region, there ensued the typical

FIG. 2. *Case 3.* Left hand of patient with hemiatrophy including thorax due to recurrent glioma invading right parietal lobe. Note pallor, smooth skin, lessening of the finger markings, and atrophy – the "lady-like" hand.

triad of flaccid paralysis, sensory loss, and atrophy.

Case 4.—Glioblastoma of the right parietal lobe, with signs of bromide intoxication. Atrophy suggested a focal lesion in spite of clouded sensorium.

A 63 year old white woman was admitted to Temple University Hospital on May 28, 1939 with a history of nervousness, presumably due to sudden loss of hearing three weeks previously. For seven days prior to admission she had experienced numbness of the left arm and foot. For several weeks she had been taking large doses of a bromide sedative to control her "nervous condition."

Examination: The patient was drowsy, with thick speech and clouded sensorium. Fundus oculi showed no choking of the disks. There was mild left facial weakness, very mild left weakness with hypotonia, sensory loss, "lady-like" hand, and softness of the muscles of the left upper limb. The deep reflexes were only mildly increased on the left side without Hoffman or Babinski signs.

Clinical course: There was a rapid progressive increase in the left-sided paralysis, sensory loss, and wasting. Headache was a late complaint. The spinal pressure was 12 mm. of mercury. A roentgen study of the skull revealed shifting of the pineal gland 5 mm. to the left.

A diagnosis of a deep-seated glioma in the right parietal lobe was made. It was felt that neither a pneumoencephalogram nor an operative procedure was indicated, due to rapid progression in the clinical picture. The patient died on June 8, 11 days after admission. Autopsy revealed a spongioblastoma bipolare in the right parietal lobe in the subcortical region.

Comment: In this case the skin and muscle changes, although mild, were of diagnostic value in directing attention to a focal lesion despite the obvious symptoms of bromide intoxication. The rapid progression of mental, motor, and sensory loss, out of proportion to the atrophy, was interpreted as a deep-seated glioma rather than one with a superficial location, which was corroborated at autopsy.

Case 5.—Glioma of parietal lobe with clinical picture of cerebral vascular lesion. Progression of atrophy a diagnostic feature in differential diagnosis.

A 69 year old white man was admitted to Einstein Medical Center on October 16, 1952 with a history of progressive speech difficulty and mental changes.

Examination: There were retinal signs of hypertension, grade 3. The electrocardiogram showed a right bundle branch block. Neurologic findings included the following: receptive aphasia, apathy, and anasognosia of the right side of the body; right central facial weakness, hypotonia, and mild motor impairment in the right arm; diminished biceps and triceps reflexes on the right side. The skin of the right hand was smooth and glossy with moderate atrophy of the interossei and forearm muscles.

A diagnosis of a focal lesion of the left parietotemporal region was made on the basis of clinical findings without arteriographic or pneumoencephalographic data. (Arteriography was attempted without success.)

Operation: A cellular astrocytoma in the left parietal region was found at operation on November 11, 1952.

Comment: This patient was examined by several members of the neurologic service. One insisted on the diagnosis of a cerebral vascular lesion, while another suspected a space-taking lesion. Both examiners overlooked the muscle and skin changes. While various laboratory studies strongly indicated a vascular pathology in view of the advanced cardiovascular disease, the rapid increase in atrophy and mental dullness with minimal motor impairment were interpreted in favor of an expanding lesion. This was corroborated at operation.

Case 6.—Glioma of the left temporal lobe invading the parietal region with resultant triad of flaccid hemiparesis, atrophy, and sensory loss.

A 44 year old white man was admitted to Temple University Hospital on April 5, 1938 with a history of headaches and aphasia of five weeks' duration. A glioblastoma was removed from the left postsuperior temporal gyrus.

On November 18, 1938 he was readmitted with a right hemiparesis, cortical sensory loss, and well-marked atrophy of the right side of the body. A diagnosis of a recurrence of the glioma with extension into the left parietal lobe was made. After a series of deep x-ray treatments, he was discharged from the hospital.

Comment: Although operation revealed a glioblastoma invading the superior temporal

lobe, there were no objective signs of parietal involvement at that time. Recurrence of the tumor with invasion of the parietal lobe resulted in the typical triad of flaccid paralysis, sensory loss, and atrophy affecting the right side of the body, including the trunk and face.

Case 7.—Metastatic lesions causing brachial plexus syndrome with superimposed atrophy in the same limb due to parietal involvement.

A 36 year old white man was admitted to Temple University Hospital February 9, 1943 with the diagnosis of a metastatic malignancy of the lung and metastatic lesions of the seventh and eighth cervical roots on the right, which produced atrophy and motor and sensory changes resembling an ulnar nerve syndrome.

About a month after admission, focal sensory and motor seizures of the right face and upper limb developed with progressive flaccid weakness of the right upper limb, sensory loss including astereognosis, and muscular atrophy of the entire right upper limb. Measurements at the level of the axilla were right 21 cm., left 24 cm.; level of right midarm 20 cm., left 24 cm.; right midforearm 21½ cm., left 25 cm.

Clinical course: The patient's condition progressed rapidly with mixed aphasia, flaccid hemiplegia, and intense wasting of the muscles of the right side of the body including the face (figure 3). Death occurred three months after onset of the condition.

Postmortem examination showed carcinomatosis of the lungs with metastatic lesions in the cervical spine implicating the roots of the lower brachial plexus on the right side, and metastatic carcinoma with cystic degeneration of the left temporoparietal lobe.

Comment: The initial findings in this case indicated an ulnar nerve syndrome due to a metastatic lesion in the lower brachial plexus. While the progression in the atrophy and motor and sensory loss could have been explained on the basis of an extension of the metastatic process to the entire brachial plexus, these symptoms, when viewed in the light of focal seizures, were considered characteristic of another metastatic lesion in the contralateral parietal lobe, which was verified at autopsy.

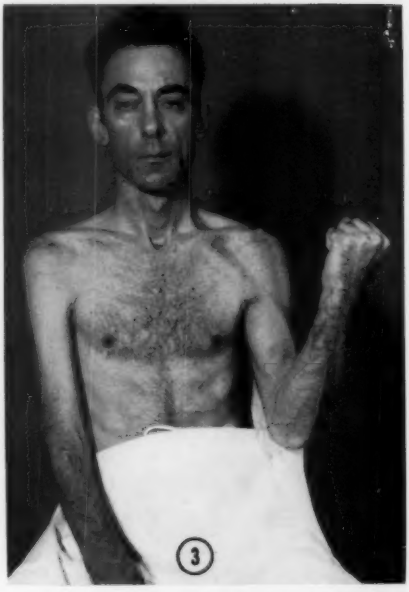

FIG. 3. *Case 7.* Flaccid amyotrophy due to metastatic lesions in left parietal lobe and right lower brachial plexus.

Case 8.—Metastatic lesion in the upper cervical roots and contralateral parietal lobe. Atrophy was a diagnostic sign in detecting a focal cerebral lesion in a patient thought to be schizophrenic.

A 38 year old white man was admitted to Temple University Hospital on July 28, 1938 with a history of headaches and pain in back of neck, which had increased progressively for a period of six months. He was reported to have had a "spell" on the way to the hospital, followed by maniacal excitement requiring physical restraint. A plaster of paris cast was applied to the neck to control pain.

Clinical course: During hospitalization the patient was often confused and disoriented. Four weeks after admission, a psychiatrist diagnosed the patient as schizophrenic and recommended removal of the cast and transference to a mental hospital.

The author was attracted to the patient's bedside by his bizarre position. He was in the center of the bed, his head resting on his chest, with arms and legs sharply flexed (fetal position). While the patient was being raised to the head of the bed, his head flopped in all

directions and he complained of severe pain radiating along the second and third cervical dermatomes on the left side. Examination disclosed marked wasting of the muscles of the entire left side, including the face, shoulder girdle, and pectoral muscles. The skin of the left hand was smooth, velvety, and colder than the right. There was left central facial weakness, left hemiparesis, and sensory loss including astereognosis. In addition, there was analgesia in the second and third cervical dermatomes on the left and motor paralysis of the flexors and extensors of the head.

Comment: This patient, diagnosed as a schizophrenic, was scheduled for transfer to a mental hospital. Examination was purely accidental, induced by the patient's bizarre position in bed. Detection of the atrophy led to a careful neurologic examination that disclosed evidence of two distinct lesions, one affecting the upper cervical roots on the left side, and the other the right parietal cortex. This was verified at necropsy.

Case 9.—Metastatic lesion in the right parietal lobe with weakness and atrophy in the left leg.

A 44 year old white woman was admitted to Temple University Hospital on February 17, 1938 with a history of focal seizures, and weakness and stiffness of the left leg which had been progressively increasing for a period of one year. Two months prior to admission the patient complained of right-sided headaches.

Examination: The optic fundi showed four diopters of choking of disks, spastic paralysis of the left leg with increased patellar reflexes, ankle clonus, and Babinski sign. There was awkwardness in the fine movements of the fingers in the left hand, but motor power was unimpaired. Astereognosis was present in the left hand. A striking feature was the marked atrophy of the muscles of the left leg and to a lesser extent in the arm. The skin of the left hand was pale, smooth, and glossy. The pineal gland was displaced to the left side. A pneumoencephalogram was technically unsatisfactory.

Operation: A mass lesion in the right superior parietal lobe, about "the size of a silver half dollar," was removed. This later proved to be a metastatic hypernephroma.

Case 10.—Glioma of the right parietal lobe with two negative arteriograms and two negative pneumoencephalograms. Atrophy of diagnostic localizing value an aid in directing accurate operative exposure over parietal area.

A 46 year old colored man was admitted to Temple University Hospital with the history of left-sided jacksonian seizures of two years' duration. Arteriograms and pneumoencephalograms on two different occasions several months previously were negative; the last study was two months prior to admission. The seizures began with clonic contractions of the face and traveled down to the left arm and leg. Two weeks prior to admission there ensued headaches, weakness, and atrophy of the left arm and leg.

Examination: There was slow cerebration and drowsiness. The optic fundi showed a suggestive blurring of the edges of the disks, mild left central facial weakness with left hemiparesis, and hyperactive deep reflexes without Hoffman and Babinski signs. Sensory examination was difficult to evaluate due to the clouded sensorium. However, there was a suggestive extinction phenomenon on the left side. The striking feature was atrophy of the left side of the body, particularly the shoulder and thigh muscles (figure 4). The skin of the left hand was smooth, glossy, with ironing out of the finger markings. The electroencephalogram was interpreted as showing a "focus in the right hemisphere, affecting chiefly the motor area or its vicinity." A presumptive diagnosis of an astrocytoma of the right parietal lobe was made.

Operation was performed on May 1, 1953 with two-thirds of the exposure centered behind the rolandic fissure and one-third in front of the fissure. No signs of tumor were encountered by probing until a hard mass was discovered in the postparietal area. The tumor, an astrocytoma, extended subcortically throughout the parietal lobe into the frontal area (figure 5).

Clinical course: The patient improved rapidly. Within a week he was able to stand and there was improvement in the motor power of the upper limb, but the atrophy on the left side progressed. Ligation of the right carotid artery was done on May 13, 1953 with little evidence of increase in the motor loss.

Comment: In this case the atrophy was of diagnostic localizing value in favor of a parietal lesion, in spite of the fact that the clinical picture of jacksonian motor seizures and progressive hemiparesis pointed to the precen-

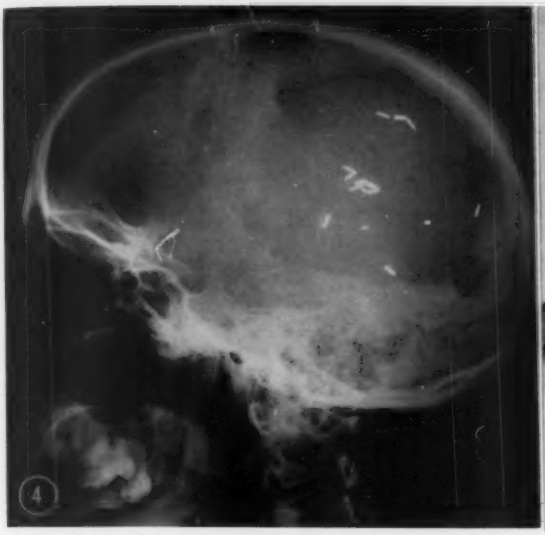

FIG. 4. *Case 10.* Postoperative examination of skull, showing bone defect and site of tumor outlined by metallic clips.

FIG. 5. Atrophy of left arm and leg due to glioma of right parietal lobe.

TABLE 2

GROUP 2–INFANTILE CEREBRAL LESIONS WITH PNEUMOENCEPHALOGRAPHIC FINDINGS. SIX ILLUSTRATIVE CASES SHOWING VARIATIONS IN THE CLINICAL PICTURE.

Case No.	*Sex*	*Age*	*Onset*	*Clinical picture*	*Findings*
11	M	46	Birth	Convulsions, smallness of upper limb, atrophy but normal length in lower limb	Porencephalic cystic defect in frontal and parietal lobes
12	M	17	Birth	Convulsions at 7 years. Right spastic hemiplegia with hemiatrophy, smallness limited to upper limb	Porencephalic cystic defect in left frontal and parietal areas
13	F	56	Childhood "polio"	Convulsions, psychotic episodes, atrophy and smallness of right leg	Discrete porencephalic defect in upper postparietal area
14	M	20	14 months of age, "polio" or "influenzal meningitis"	Smallness limited to right leg—minimal motor impairment	Porencephalic cyst in left paracentral region
15	F	23	"Measles encephalitis" at 8 years of age	Smallness limited to left arm. Pyramidal tract signs in lower extremity without atrophy or shortening	Cortical atrophy in right frontoparietal region. Occlusion of internal carotid artery by arteriography
16	F	22	At 6 years, compound fracture of left parietal bone with adjacent brain abscess	Mental retardation, jacksonian convulsions at 12 years, right hemiatrophy, hemiparesis, and sensory loss	Porencephalic enlargement of left lateral ventricle with meningocortical scar in postparietal area

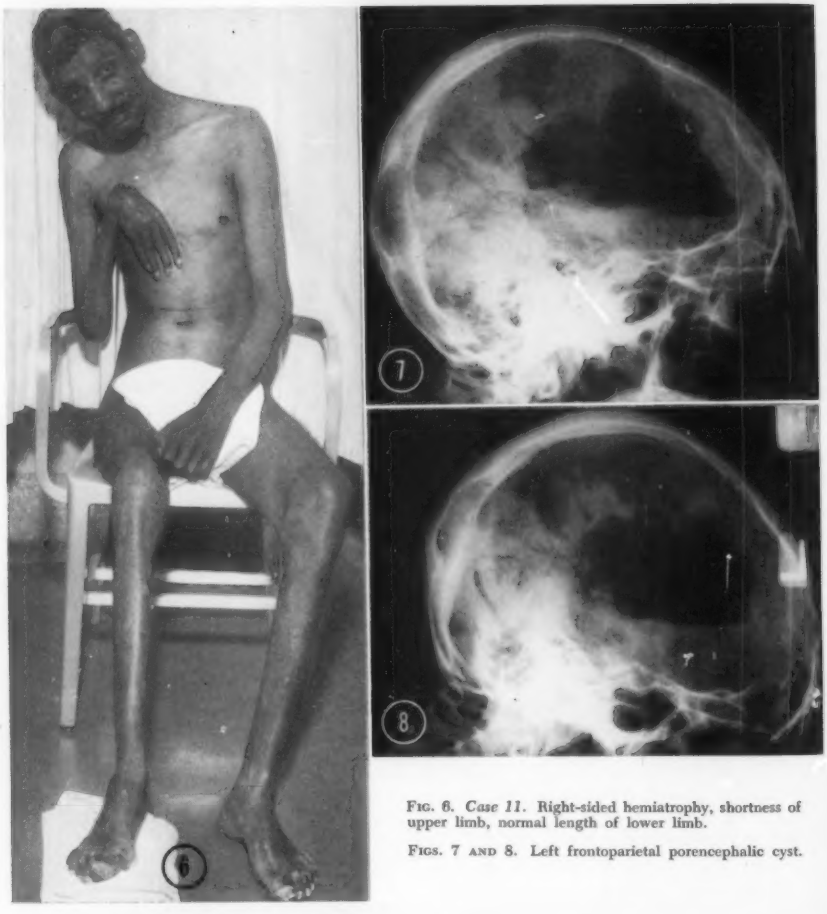

FIG. 6. *Case 11.* Right-sided hemiatrophy, shortness of upper limb, normal length of lower limb.

FIGS. 7 AND 8. Left frontoparietal porencephalic cyst.

tral gyrus. This differential diagnosis was important since it was responsible for centering the operative exposure over the parietal lobe. This was fortunate since evidence of tumor was detected only when the postparietal region was explored. In the usual exposure for a tumor in the motor region, this lesion in all probability would have been overlooked.

GROUP 2 consisted of 30 cases of infantile cerebral lesions. Illustrative cases are summarized here to show variations in the atrophy and pneumoencephalographic findings (table 2).

Case 11.—Left frontoparietal porencephalic cyst with right-sided hemiatrophy, shortness of the upper limb, and normal length of the lower limb.

A 46 year old man was born with paralysis of the right side of the body. He had been subject to convulsive seizures for many years. He was admitted to Philadelphia General Hospital in November 1952 with a history of re-

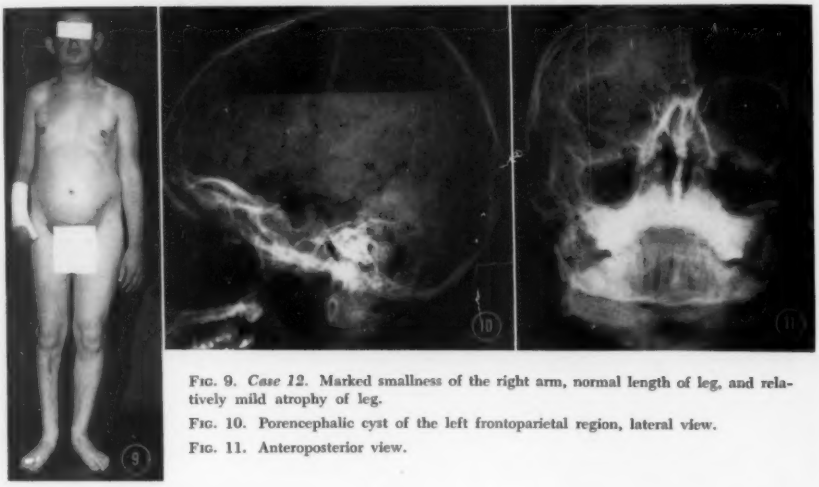

FIG. 9. *Case 12.* Marked smallness of the right arm, normal length of leg, and relatively mild atrophy of leg.

FIG. 10. Porencephalic cyst of the left frontoparietal region, lateral view.

FIG. 11. Anteroposterior view.

cent onset of repeated strokes on the left side of the body.

Examination revealed a right spastic hemiplegia with flexor contracture at the elbow, shortness and atrophy of the upper limb, and atrophy of the muscles of the lower limb, but without decrease in growth (figure 6). On the left side of the body there was spastic hemiparesis with increased reflexes and Hoffman and Babinski signs. The pneumoencephalogram showed a marked porencephalic defect extending from the frontal to the postparietal area (figures 7 and 8).

Comment: The significant feature in this case was the decrease in growth limited to the upper limb. The lower limb, while atrophic, was of normal length. This would suggest that the mechanism responsible for growth changes is somewhat different from that producing muscular atrophy, although usually both of these trophic changes occur together from involvement of the postrolandic region.

Case 12.—Porencephalic cyst of the left frontoparietal region with smallness of right arm and normal length of leg.

A 17 year old white boy was admitted to Temple University Hospital on September 25, 1946 with a history of paralysis of the right side of the body, which presumably had resulted from a difficult forceps delivery at birth. Convulsive seizures had begun at the age of seven.

Examination revealed a right spastic hemiplegia with hyperactive deep reflexes and Babinski sign. There was moderate atrophy and noticeable smallness of the right upper limb, less marked wasting and practically no shortening in the lower extremity (figure 9). The pneumoencephalogram revealed a large porencephalic cystic lesion in the frontal as well as in the parietal region (figures 10 and 11).

Comment: In this case the striking feature was the marked growth retardation of the right upper limb, with practically no shortening in the lower limb. Muscle wasting in the lower extremity was much less pronounced than in the upper limb.

Case 13.—Porencephalic cyst in the left upper postparietal area with atrophy of the contralateral lower extremity, considered a residual of poliomyelitis.

A 56 year old woman was admitted to Philadelphia General Hospital for the fifth time on May 4, 1953. On earlier admissions the diagnoses were recorded as "progressive cerebral thrombosis," "involutional melancholia with auditory hallucinations," and "manic-depressive psychosis of the paranoid type." The patient had been having convulsive seizures for many years. There was a vague history of "infantile

FIG. 12. *Case 13.* Atrophy of right leg resembling residual anterior poliomyelitis.

FIG. 13. Porencephalic cyst in left postparietal area.

paralysis" in childhood,,which resulted in weakness of the right leg.

Examination: The patient was confused, disoriented, and had auditory hallucinations. The striking positive feature was atrophy of the right lower extremity, especially the leg, with contracture deformity of the foot (figure 12). The right patellar reflex was hyperactive; the achilles response was absent. Plantar stimulation elicited a very suggestive Babinski sign, which was difficult to interpret due to toe deformity. Electrical examination of the muscles of the leg (thigh muscles were not examined) showed scattered signs of degeneration suggestive of lower motor neuron disease. The electroencephalogram showed "diffuse abnormalities with a suggestion of an irritating lesion in the left hemisphere." A pneumoencephalogram revealed a "large porencephalic cyst in the left upper postparietal portion of the cerebral hemisphere which was continuous with the lateral ventricle of the same side" (figure 13).

Comment: This patient was considered an epileptic who had had several psychotic epi-

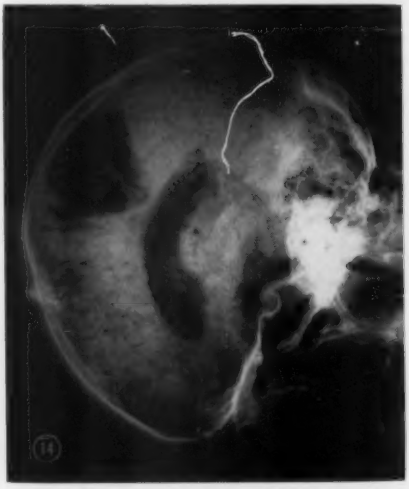

FIG. 14. *Case 14.* Porencephalic cyst in the right paracentral region, with clinical picture of atrophy of left leg and minimal motor impairment.

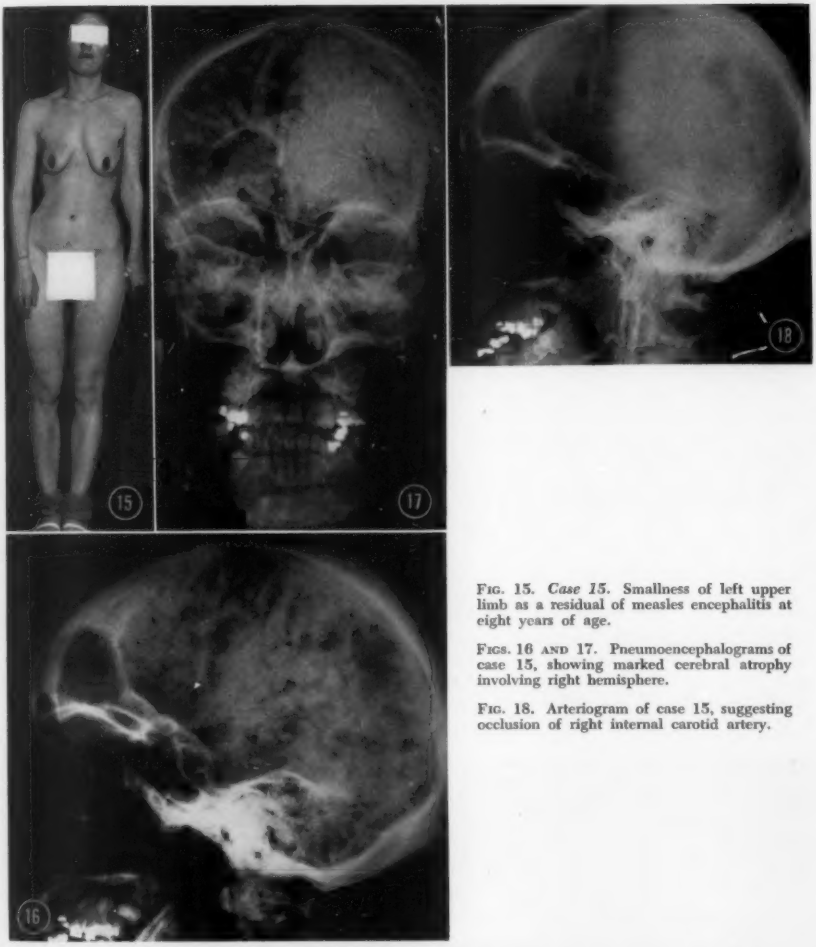

FIG. 15. *Case 15.* Smallness of left upper limb as a residual of measles encephalitis at eight years of age.

FIGS. 16 AND 17. Pneumoencephalograms of case 15, showing marked cerebral atrophy involving right hemisphere.

FIG. 18. Arteriogram of case 15, suggesting occlusion of right internal carotid artery.

sodes. Atrophy of the leg and deformity of the right foot strongly resembled a residual of an old neglected poliomyelitis. There were other signs, particularly in view of the convulsive seizures, which suggested a parietal lesion. Pneumoencephalography revealed a cystic lesion in the upper left postparietal area, which corresponded with the leg area and could have been a factor in atrophy of the contralateral extremity. This lesion could also explain the patient's convulsive seizures. Possibly it was a factor in the psychotic episodes on the basis of a postconvulsive psychotic reaction.

Case 14.—Porencephalic cyst in the upper parietal lobe with atrophy in the contralateral extremity and minimal motor impairment.

A 20 year old man was admitted to Temple University Hospital on September 9, 1948 with the chief complaint of convulsions of two years' duration. At 14 months of age it was presumed

he had poliomyelitis or influenzal meningitis, which resulted in weakness of the left lower extremity. Motor power had apparently improved and he walked without difficulty.

Examination disclosed a relatively mild motor weakness in the left lower extremity, with slightly increased knee jerk and an equivocal Babinski sign. Marked atrophy of the entire left lower extremity, particularly the leg, was evident.

Pneumoencephalography disclosed "a sharply demarcated air-containing cavity, measuring 5 cm. in diameter, situated in the right midparietal area near the vortex reaching to the midline (figure 14). The right ventricle appeared larger than the left and also appeared to be retracted very slightly toward the above noted cavity. In spite of this slight asymmetry, there was no displacement of the midline structures."

Comment: This patient, with a focal porencephalic cyst in the region of the right paracentral area, exhibited marked atrophy in the contralateral extremity. The minimal sensory and motor disturbance was of particular interest. As in the previous case, this is another example of a focal muscular atrophy, presumably due to early poliomyelitis, that was proved to have a corresponding lesion in the contralateral parietal lobe. Discovery of the discrete lesion was accidental, since pneumoencephalography was carried out primarily for study of the convulsive state.

Case 15.—Infantile cerebral hemiplegia following measles encephalitis at age eight. Growth retardation with muscular atrophy limited to the upper limb.

A 23 year old white woman was admitted to Temple University Hospital on January 6, 1953 with complaints of pain in the left arm and leg, right-sided headaches, and convulsive seizures. She was presumed to have had measles encephalitis at age eight, which left her with a paralysis of the left side of the body. This had gradually improved, especially in the lower limb.

Examination showed left homonymous hemianopsia, mild left central facial weakness, and spastic paresis of the left side of the body with smallness and atrophy limited to the upper limb (figure 15). The left leg showed mild motor impairment, chiefly in the plantar flexion of the toes, with hyperactive knee jerk and positive Babinski sign. There was hypesthesia in the left upper extremity, with impaired touch sensation of the fingers, graphesthesia, and astereognosis.

The pneumoencephalogram showed "a marked cerebral atrophy involving the right cerebral hemisphere, with asymmetry of the bones of the skull and compensatory enlargement of the bones of the skull on the right side, as well as the air sinuses due to marked decrease in brain substance on the right side" (figures 16 and 17). A right carotid angiogram disclosed faint visualization of the right carotid artery as far

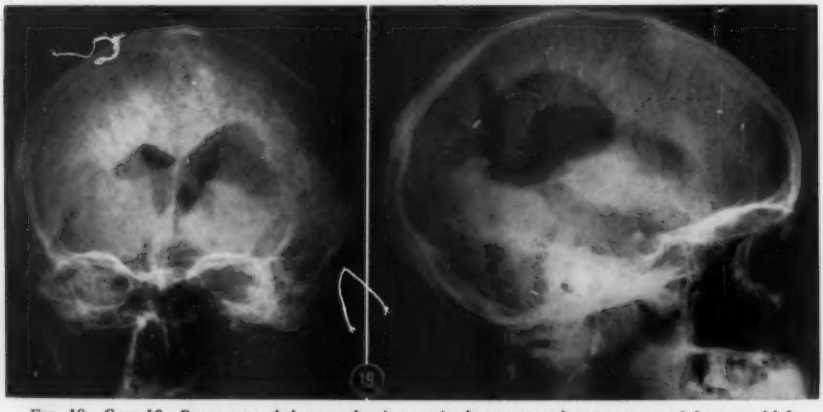

FIG. 19. *Case 16.* Pneumoencephalogram showing cystic changes secondary to compound fracture of left parietal bone and brain abscess. Clinical picture of jacksonian seizures and right-sided hemiatrophy.

as the sella turcica. There was no visualization of the intracranial branches of the internal carotid artery. "This was evidence of an actual occlusion of the intracranial portion of the internal carotid artery or marked delay through it" (figure 18).

Comment: The important feature in this case was the limitation of growth retardation and muscular atrophy to the upper extremity, presumably due to an occlusion of the internal carotid artery which occurred following measles. While there was obvious evidence of pyramidal tract disturbance in the lower limb, there was neither atrophy nor shortening. This may be explained by the fact that the leg area in the paracentral lobe was unaffected since it is supplied by the anterior cerebral artery. It also tends to refute the importance of the pyramidal tract in the mechanism of atrophy. The relatively late occurrence of the brain lesion at the age of eight years should be emphasized. In Penfield's and Robertson's cases of infantile cortical lesions, smallness of the limb resulted from lesions occurring before the age of three years.

Case 16.—Compound fracture of left parietal bone with complicating brain abscess. Jacksonian seizures with right hemiatrophy and smallness of the right arm and leg.

A 22 year old white woman was admitted to Temple University Hospital on October 1, 1944 with a history of having sustained a compound fracture of the left parietal bone at the age of six years, when she was struck by an automobile. Subsequently, an infection of the wound developed, with an underlying brain abscess which was drained. Immediately preceding the operation she became aphasic and had a loss of motor power in the right arm and leg. Following operation, speech gradually returned with improvement in the motor power of the right side of the body.

Two years following the accident, she began to suffer from convulsive seizures which began with a numb feeling in the right hand, followed by jacksonian seizures of the entire right side of the body. Seizures occurred frequently despite the use of various analeptic drugs.

Examination disclosed a mentally retarded patient. There was right spastic hemiparesis, more marked in the upper extremity, and hyperactive deep tendon reflexes with positive Hoffman and Babinski signs. There was sensory loss with impaired touch sensation on the right side of the body. The right arm and leg were atrophic and shortened. The skin of the right hand and arm was shiny and smooth "showing the typical changes found in parietal lobe lesions."

Roentgen examination of the skull showed an "old defect in the left parietal bone, measuring 5 x 4 cm., with smoth margins except for a little roughening along the posterior inferior border."

A pneumoencephalogram on September 21, 1944 disclosed a porencephalic-like enlargement of the lateral horn of the ventricle through its posterior half, where it lay beneath the old bone defect in the skull (figure 19). The midline structures were slightly shifted to the right. It was concluded from this study that there was atrophy and porencephalic enlargement of the

TABLE 3

ANALYSIS OF FIFTY CASES OF HEMIPLEGIA OF VASCULAR ORIGIN

	Number	*Paralysis*	*Sensory Loss*
With atrophy	28	Flaccid	Present—with astereognosis
Without atrophy	22	Spastic	No

THREE ILLUSTRATIVE CASES WITH ATROPHY SHOWING PARIETAL INVOLVEMENT

Case No.	*Sex*	*Age*	*Clinical picture*	*Laboratory findings*
17	M	54	Sudden onset of flaccid hemiplegia, atrophy, sensory loss	X-ray of shoulder demonstrating subluxation. Arteriogram showing occlusion of middle cerebral artery.
18	M	64	Sudden onset, flaccid hemiplegia, sensory loss, hemiatrophy, including face as early as 4th day. Sensory defect with astereognosis.	Occlusion of middle cerebral artery.
19	M	41	Burning pain of left side of body, hemiparesis, sensory loss, atrophy	Air encephalogram shows atrophy of right frontoparietal region

left lateral ventricle, secondary to previous head injury with contusion of the brain.

Comment: In this patient with evidence of injury and infection of the parietal lobe at six years of age, there resulted the clinical picture of atrophy and smallness of the contralateral arm and leg. This conforms with the pattern of our other cases of infantile cerebral hemiplegia due to other types of lesions involving the parietal region.

GROUP 3 consisted of 50 cases of hemiplegia divided into two subgroups. Twenty-eight cases with atrophy were associated with sensory loss and hypotonia, usually at the shoulder, while 22 cases without atrophy had no sensory loss and the paralysis was usually spastic in type. Some of the patients in the latter group had been hemiplegic for more than four years.

The following illustrative cases of the first subgroup are designed to demonstrate the similarity of the clinical picture with the parietomotor syndrome due to tumors and other lesions invading the parietal lobe.

Case 17.—Thrombosis of middle cerebral artery simulating a space-occupying lesion. Atrophy of the left upper extremity with subluxation of left shoulder.

A 54 year old colored man was admitted to Temple University Hospital October 19, 1952 with the history of having engaged in a fist-fight the previous night and awakening the following morning with paralysis of the entire left side of the body.

Examination disclosed a complete left flaccid hemiplegia, including the face, with absence of all deep tendon reflexes.

Roentgen examination of the skull was normal; the pineal gland was not visualized. An arteriogram, three days after admission, revealed a complete occlusion of the middle cerebral artery on the right side (figures 20 and 21).

Clinical course: The day following admission pneumonitis set in which was controlled by antibiotic therapy. On the sixteenth day a trophic edema of the left leg appeared. Six weeks after admission there was a complete flaccid hemiplegia with loss of deep reflexes, sensory loss including astereognosis, and well-marked atrophy of the entire left upper limb (figure 22) and, to a lesser degree, the lower extremity. The circumference in the middle of the left arm was 2 cm. less than on the right side; the forearm was 2.4 cm. less. The trophic edema of the leg had increased, also involving the left hand.

Wasting of the muscles about the shoulder was so pronounced that the head of the humerus was palpated outside of the glenoid fossa. Roentgen examination corroborated the diagnosis of subluxation of the shoulder (figure 23).

Biopsy examination of the atrophic muscle was reported as follows: "fibers have lost fine striations and appear either granular or vacuolated. A few fibers show fragmentation and longitudinal fibrillation" (figure 24).

Comment: The history of head injury the day before admission suggested a subdural hemorrhage. The clinical picture of flaccid paralysis with depressed deep reflexes, sensory loss, and atrophy corresponded to the typical picture seen in space-occupying parietomotor lesions. This localization was proved by the arteriogram which showed a complete occlusion of the middle cerebral artery. Biopsy of the atrophic muscles disclosed well-marked pathologic changes. It is to be emphasized that the flaccidity and tissue atrophy about the left shoulder was so pronounced that marked subluxation resulted. This could only be demonstrated when the roentgen study was carried out with the patient in the upright position, the arm hanging to the side. In the recumbent position, the subluxation was not seen.

Case 18.—Occlusion of the middle cerebral artery with contralateral flaccid paralysis and atrophy including the face, simulating a peripheral type of palsy.

A 64 year old white man was admitted to Philadelphia General Hospital February 25, 1953 with the history of a fall 24 hours previously which rendered him unconscious for about two minutes. Immediately thereafter, there was paralysis of the right arm and leg. He was known as a hypertensive for at least four years. There were four previous admissions for acute alcoholism.

Four days after admission, examination disclosed a marked facial paralysis with a "sinking-in" of the right side of the face, drooping of

FIGS. 20 AND 21. *Case 17.* Arteriograms showing occlusion of right middle cerebral artery.
FIG. 22. Left-sided flaccid amyotrophy.
FIG. 23. Subluxation of the left shoulder due to flaccidity and wasting of muscles.
FIG. 24. Biopsy of atrophic muscle, showing loss of striations of muscle fibers, vacuolation, and fragmentation.

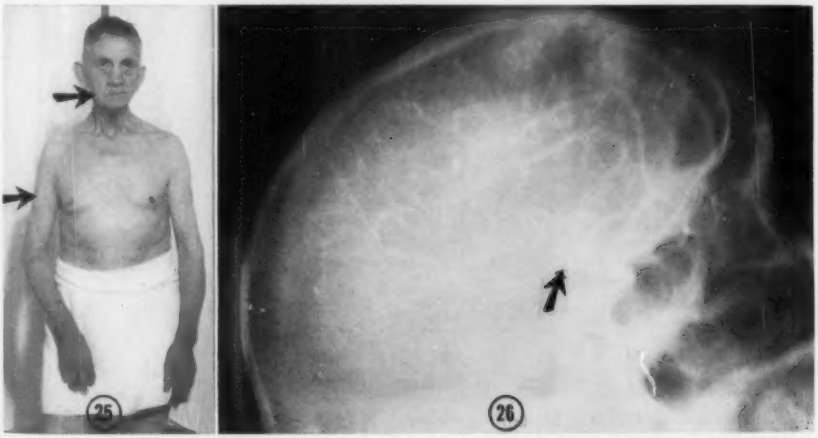

FIG. 25. *Case 18.* Flaccid paralysis of right upper limb with atrophy of arm and face, resembling peripheral facial palsy. Note deviation of right nipple downward and outward due to flaccidity of overlying muscles.
FIG. 26. Arteriogram showing occlusion of left middle cerebral artery.

the right corner of the mouth, widening of the palpebral fissure, ectropian with wasting, drooling of saliva, and flabbiness and wasting of facial muscles closely resembling peripheral facial palsy. There was a flaccid right hemiplegia with extinction phenomenon, cortical sensory loss, and astereognosis. The right nipple was deviated downward and outward due to the flaccidity of the pectoral muscles. There was atrophy in the upper extremity chiefly in the shoulder, much less in the arm, and absent in the hand (figure 25). Abdominal reflexes were absent on the right side. A presumptive diagnosis of a left parietomotor lesion was postulated, probably vascular in origin. Arteriogram disclosed an occlusion of the middle cerebral artery on the left side (figure 26).

Clinical course: The patient gradually improved, and the power of the leg returned rapidly. On July 14, 1953, almost five months after admission to the hospital, there was spasticity at the elbow, hypotonia at the shoulder, and advanced wasting of the muscles, particularly about the shoulder.

Comment: The feature in this case was the early wasting of the muscles of the face and upper limb which was detected on the fourth day of illness. As in the previous case, arteriogram disclosed a lesion in the frontoparietal area due to an occlusion of the middle cerebral artery.

Case 19.—Atrophy of the right frontoparietal region, with right-sided paralysis and muscular atrophy.

A 41 year old colored man was admitted to Temple University Hospital March 30, 1953 with the chief complaints of burning pain on the left side of the face and body, and weakness of the left leg and arm. In April 1948 he was treated at another hospital for "cerebral apoplexy," hypertension, and left hemiplegia. In 1941 he was rejected from service in the armed forces because of hypertension.

Examination revealed a spastic paralysis of the left arm and leg with hyperactive deep reflexes, ankle clonus, and positive Babinski sign. There was well-marked atrophy of the left side, particularly at the shoulder (figure 27).

Pneumoencephalogram revealed a "communicating hydrocephalus with the right ventricle much more markedly dilated (figure 28). Findings were interpreted as atrophy of the left cerebrum of a diffuse nature, presumably re-

FIG. 27. *Case 19.* Left-sided hemiparesis with atrophy of left arm.

FIG. 28. Pneumoencephalogram showing communicating hydrocephalus with the right ventricle much more markedly dilated, presumably due to diffuse atrophy of left cerebrum resulting from an old vascular accident.

lated to the previous vascular accident on that side. There was evidence of obliterative arachnoiditis over the cerebral hemisphere, bilaterally, which contributes to the hydrocephalus and is probably on the basis of previous subarachnoid hemorrhage."

The electrocardiogram disclosed myocardial disease and left ventricular hypertrophy.

Comment: This relatively young man had his first cerebral vascular accident at the age of 36 years. The encephalogram demonstrates that the lesion was cortical in the frontoparietal area rather than in the internal capsule.

COMMENT

Evidence has been presented from personal observations and from study of the literature which indicates that diverse lesions involving the parietal lobe are associated with muscular atrophy and other trophic changes in the contralateral parts of the body. From the practical clinical standpoint the atrophy has proved to be a consistently reliable sign in diagnosis. Great emphasis is placed on the importance of careful and repeated systematic examinations of the skin and muscles for evidence of atrophy, since these are so frequently overlooked in routine examinations. On numerous occasions the author has demonstrated to students and residents patients with cerebral lesions showing well-marked wasting of muscles, and has called their attention to the absence of any record of this finding on the hospital charts. Such oversight may be due to several reasons: 1) difficulty of undressing paralyzed patients, 2) laxity in recording clinical findings once the diagnosis is established, usually by laboratory methods, and 3) emphasis on vital signs following surgery and ablations with relatively minor attention to recording clinical features. Obviously, alertness for atrophy throughout the clinical course of a cerebral disorder is essential for proper evaluation of the incidence and clinical significance of this sign in brain lesions.

One of the first clues for recognition of the wasting may be the appearance of the hand. The skin is pale, soft, and glossy with less definite finger markings, and it often feels colder than the opposite hand. Due to changes in the subcutaneous tissue, the entire hand may appear smaller and more delicately formed, having a "ladylike" appearance. The wasting of muscles can be detected more readily by palpation than by inspection. Even in the early phase the muscles feel soft and boggy, and the bony structures covered by the softened muscles are more readily palpated. In advanced cases the wasting may resemble that found in diseases of the spinal cord or peripheral neuron. The electrical reactions show a hypoexcitability to faradic and galvanic stimulation, but no qualitative changes.

The shoulder group and the small muscles of the hand seem to be the earliest and most severely affected. Not infrequently, an edema of the hand may disguise the underlying atrophy, but at times this may be removed by elevating the arm. While the upper limb is most frequently involved, we have described several cases in which the atrophy was limited to one or both legs. In case 1 the clinical picture of coldness, sweating, and wasting of the muscles in one leg and paralysis of the toes in the other led to a diagnosis of residual poliomyelitis before the true nature of the lesion, a parasagittal meningioma, was discovered. We have observed that in wasting of the extremities, the thorax, face, and tongue can also be similarly affected. Garcin, Deparis, and Hadj-Dimo[34] described severe hemiatrophy, including the trunk, in an adult which resembled

the pattern seen in infantile cerebral hemiplegia. We have observed several cases of parietal tumor showing a unilateral facial atrophy usually associated with wasting of one upper limb. One wonders whether some of the cases of facial hemiatrophy associated with epilepsy as reported in the literature may not be due to lesions in the parietal cortex. In one such case reported by Donley,[35] Penfield and Robertson[16] found sufficient evidence to justify the assumption of a lesion in the postcentral cortex in one hemisphere.

As a rule the atrophy is moderate, but to a great extent the degree of muscle wasting depends upon the type of lesion. In traumatic cases the wasting comes on rapidly, reaches its peak early, and remains stationary. In cerebral vascular lesions, the atrophy may become less pronounced with the improvement in the motor and sensory functions. We have seen patients with "strokes" in whom mild wasting of muscles or skin changes were the only residuals of a former hemiplegia. The most intense wasting was noted in expanding cortical lesions affecting both the parietal region and the motor pathways. In such cases the wasting was so marked as to simulate spinal cord disease. In two patients with meningioma, the atrophy disappeared entirely after removal of the tumor.

A question is often raised concerning the time interval before appearance of the atrophy. In cases of hemiplegia, some authors suggest a two week period from the onset of the vascular lesion. Borgherini[36] has noted atrophy within three days. We have seen wasting in paralyzed extremities appear within 48 hours following surgical injury to the parietal lobe. In "strokes" the atrophy was observed in patients as early as the fourth day from the onset of the vascular lesion.

Various theories have been advanced to explain the mechanism of cerebral amyotrophy, such as changes in the anterior horn cells,[37] peripheral neuritis,[38] and arthropathy.[39] While these and other factors may play a role in certain cases of late atrophy in hemiplegia, they do not explain our cases of early atrophy. That joint disease may be the end result of the atrophy rather than its cause is well demonstrated by several of our cases where flaccidity and wasting of the muscles were so pronounced as to produce a subluxation at the shoulder. The constant pull and irritation of the structures about the joint could readily result in synovitis and arthritis.

It has long been maintained that the cerebral cortex exerts a trophic influence upon the contralateral parts of the body. Some authors point to an implication of cerebral vasomotor centers, while others insist upon a true trophic center with specific fibers distinct from the motor pathways. Von Monakow[40] postulated a simultaneous reduction of the sensory, motor, and vasomotor functions.

Our own studies indicate that lesions in the parietal region cause a disturbance of trophic function resulting in atrophy and changes in the skin of the contralateral peripheral musculature. The precise mechanism is still undetermined. In most of our cases the atrophy was combined with mild vasomotor changes; pronounced alterations were rare and in some cases absent. The fact that hypotonia and sensory changes invariably accompanied the atrophy indicates a close relationship between them. There is further indication of such a relationship since the degree of wasting often parallels the degree of these two

symptoms, especially that of sensory loss. However, we have described cases in a previous report[1c] in which the atrophy was an isolated sign or preceded sensory as well as motor changes. Thus at the present time, we must assume that the parietal cortex has some special trophic function which is closely allied but distinct from the vasomotor and other functions of the somesthetic cortex.

From the clinical standpoint there is abundant evidence to demonstrate that atrophy is an important, if not the most significant, sign of lesions of the parietal lobe. Observation of patients with various lesions in different parts of the brain disclosed that atrophy occurred only with parietal involvement and was absent in lesions of the frontal, temporal, or occipital areas. Furthermore, when the postrolandic region was involved, either by invasion of an expanding lesion or injury from extirpation of a neighboring tumor, atrophy, together with other signs of the parietal syndrome, invariably resulted.

Additional evidence pointing to the trophic influence in the parietal cortex is the study of group 2, consisting of a series of cases of infantile cerebral lesions showing the clinical picture of infantile cerebral hemiplegia, retarded growth development, and hemiatrophy. In all of these cases the pathologic process implicated the postrolandic region. Illustrative cases are recorded to demonstrate that variations in the pattern of the growth retardation and muscular atrophy of the parts affected may depend upon the specific location of the brain lesion. In one patient, a discrete porencephalic cyst in the postparietal region was associated with a contralateral atrophy limited to the right leg which could not be differentiated from an old poliomyelitis. A similar type of lesion in the paracentral region in another patient resulted in a contralateral atrophy of the leg with only minimal pyramidal signs. In two patients with shortening of the upper limb with normal length of the lower extremity, the pneumoencephalogram showed extensive frontal as well as parietal involvement. It would appear that, with the lesions limited chiefly to the parietal lobe, the smallness of the limb was limited to the upper extremity. While pyramidal tract signs were present in the lower extremities of both patients, there was neither atrophy nor shortening. This would indicate that the pyramidal tract plays a minor role in the mechanism of the growth retardation as well as the atrophy.

In a study of group 3, observations were made on cases of hemiplegia with and without atrophy. Wasting of the muscles invariably occurred in those cases showing sensory changes and was usually absent in those without sensory loss. This combination of sensory loss and atrophy indicating a retrorolandic origin has been well demonstrated in cases 17 and 18, which showed complete occlusion of the middle cerebral artery by arteriography. Frequently, this type of case is considered to be due to a lesion in the internal capsule.

One of the objections raised against the parietal localization for the amyotrophy has been the associated pyramidal tract involvement in the clinical picture. It was this fact that led Spiller to state, in his discussion of the first preliminary report[1a] by the author in 1930, "if the parietal lobe has an influence in causation of the atrophy it must be in association with hemiplegia produced by a lesion of the pyramidal tract." Further, he

added, he knew of no case of cerebral amyotrophy to have developed as a result of a lesion confined to the parietal lobe. In a subsequent report[1b] this objection was overcome by the report of two cases of parietal lesions which, except for jacksonian seizures, showed contralateral atrophy without motor and sensory disturbances.

From a diagnostic standpoint, the atrophy has proved of great value in localization and differential diagnosis. Mention was made that atrophy was an isolated objective parietal lobe sign. In several of our cases the skin and muscle changes were the earliest evidences of a parietal lesion. A previous report[1c] of the case of a patient with an expanding gliomatous lesion in the parietal lobe was studied throughout the clinical course from the onset of the initial symptom of focal sensory and motor seizures of the face and tongue. The atrophy of the upper limb was the first objective sign and preceded the predicted occurrence of the sensory and motor changes. Although surgery was urged in this early phase, the neurosurgeon objected strenuously since the pneumoencephalogram and other studies were negative for tumor. Subsequently, there developed the typical triad of intense muscular wasting, cortical sensory loss with astereognosis, and flaccid hemiplegia. Had the atrophy been accepted as a localizing sign in the early phase of the illness, a much better result than the six month period of improvement might have ensued.

The atrophy has also been a valuable localizing sign in distinguishing lesions in the parietal lobe from those in other regions of the brain. This was of particular value in cases of psychotic and toxic patients, and also in those with clouded sensorium where an adequate sensory examination could not be carried out. In three patients with bromide intoxication, the muscular atrophy was an important sign in directing attention to a focal brain lesion which would otherwise have passed unrecognized.

In many of our patients it was difficult to distinguish between the clinical picture of brain tumor and cerebral thrombosis since the usual signs of increased intracranial pressure were absent. In nine out of ten cases of brain tumors in group 1, there was no choking of the disks when the diagnosis was made. By careful and repeated examinations of the character and progression of the atrophy in relation to the total clinical picture, it was possible to differentiate between these two conditions. For example, in case 5 one neurologist on our staff made a diagnosis of cerebral vascular lesion, while another suggested brain tumor. Both examiners failed to note changes in the skin and muscles. The observation of a rapid progression of the muscular wasting which paralleled progressive mental change, with relatively mild motor weakness in the extremities, was interpreted as indicative of a glioma in the parietal lobe, in spite of the obvious evidence of advanced cardiovascular disease. This diagnosis was verified at operation.

Muscular atrophy was also an important sign in the differential diagnosis between mass parietal lesions and syphilis of the nervous system. The progressive increase in wasting of the extremities, without progressive motor loss, pointed to a focal lesion.

In several of our patients the clinical picture was characteristic of a psychogenic disturbance. One patient was diagnosed by several members of the staff

as a typical case of hysteria. The atrophy of one extremity led to careful examination which disclosed the clinical picture of a space-occupying lesion of the parietal lobe, which proved to be a glioma at operation. In case 8, labeled schizophrenia, atrophy of the extremities led to careful study which resulted in the diagnosis of metastatic lesions in the upper cervical roots on one side and in the contralateral parietal lobe.

While the differential diagnosis between brain tumor and spinal cord and peripheral neuron disease would seem relatively easy at first sight, we have seen at least six cases of proven parietal tumors diagnosed as poliomyelitis. In three of our cases, experienced neurologists made a diagnosis of syringomyelia, which later proved to be parietal lobe tumors. In this connection, Van Bogaert[35] reported such a case which was treated as syringomyelia.

In several instances parietal amyotrophy had to be distinguished from the shoulder-hand syndrome. While a reflex spinal cord mechanism may be a factor in the latter syndrome, a postrolandic involvement of vascular origin also may play a part in certain instances. That concomitant cerebral vascular lesions occur with cardiac lesions is well known. Thus occlusion of the postcentral branch of the right middle cerebral artery in the nondominant hemisphere can produce wasting of the muscles of the left upper limb which could readily be confused with so-called shoulder-hand syndrome. Before accepting the reflex mechanism for the latter syndrome, more precise studies on the cerebral factor, as well as study of the changes in the muscles, are necessary.

The characteristic pathologic changes in the atrophied muscles of cerebral origin have been described by Marinesco[8] and later by Winkelman and Silverstein.[5] Necropsy specimens disclose a mushy, yellowish appearance of the muscles. There is a diminution in the caliber of the muscle fibers with alterations of the striations, fragmentation, or even empty sheaths. A biopsy of the atrophic muscle in case 17 showed changes similar to those previously described in necropsy specimens.

SUMMARY AND CONCLUSIONS

That amyotrophy can serve as an important sign of parietal disease is based on the following facts:

1. Atrophy was strikingly evident in patients with tumors of the parietal lobe, while it was absent in cases where the frontal, temporal, and occipital lobes were affected.

2. Atrophy appeared promptly, together with other signs of the parietal syndrome, following surgical injury of the parietal region or invasion of it by lesions expanding from adjacent areas.

3. Unilateral atrophy has occurred as an isolated sign of parietal involvement, which refuted the argument that atrophy occurs only with pyramidal tract signs.

4. Atrophy has been observed as the earliest sign of parietal involvement, preceding sensory and motor disturbances.

5. Topical localization within the parietal lobe, similar to the pattern existing in the motor or sensory cortex, is borne out by several of our cases in which the atrophy was limited to the lower limb, face, and tongue. The upper limb is most frequently involved.

6. The degree of tissue wasting depends upon the size, character, and location of the lesion. Early atrophy is more easily detected by palpation of soft bog-

gy muscles, pallor and smoothness of the skin and lessening of the finger lines — the "ladylike" hand. The most intense degree of wasting occurs in expanding cortical lesions affecting the motor pathways as well as the sensory cortex. In such instances there is a characteristic triad of atrophy, flaccid paralysis, and cortical sensory loss, especially astereognosis. The electrical reactions show a hypoexcitability to both faradic and galvanic stimulation, but no qualitative changes.

7. Subluxation at the shoulder due to muscular atrophy may produce synovitis and arthritis in hemiplegia. This fact would seem to be of therapeutic significance.

8. Abundant evidence in the old and new neurologic literature confirms the concept of parietal amyotrophy.

From the foregoing data it is concluded that amyotrophy is a significant localizing sign of great value in the diagnosis of lesions in the parietal lobe. It is especially important when studying patients with clouded sensorium on whom an accurate neurologic examination cannot be performed. To the neurosurgeon, atrophy is of value in directing an accurate operative exposure. Careful, repeated examinations for atrophy in patients with cerebral disorders cannot be too strongly emphasized.

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The weakened powers of the muscles in the affected parts is so prominent a symptom as to be very liable to mislead the inattentive, who may regard the disease as a mere consequence of constitutional debility. If this notion be pursued, and tonic medicines, and highly nutritious diet be directed, no benefit is likely to be thus obtained; since the disease depends not on general weakness, but merely on the interruption of the flow of the nervous influence to the affected parts.

James Parkinson in *An Essay on the Shaking Palsy*, published in 1817.

Effect of Reserpine Upon the Human Electroencephalogram

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THERE have been reports[1,2] of the effect of reserpine on the electroencephalogram of lower animals. These reports point out that the electrical potentials of the brain as measured through the intact scalp are unaffected by the drug until drowsiness or sleep occurs, such as might happen with large doses of reserpine or when the animal is left undisturbed.

The present study is concerned with the electroencephalograms of 26 adults who are known hypertensives. These were recorded through the intact scalp on a standard eight channel Grass electroencephalograph.

Eleven of these patients with hypertension had electroencephalograms both before and after reserpine therapy. These patients, consisting of ten females and one male, ranged in age from 22 to 62. All suffered from essential hypertension or mild to moderate hypertensive vascular disease. No cases with known cerebral vascular involvement were included. These patients received an average of 1 mg. of reserpine a day for a period of seven to eight months. Eight of these patients showed no change in their records, seven being normal before and after, and one slightly abnormal before and after reserpine therapy. In two cases, slightly abnormal records became normal after a trial on the drug, and in one other case an abnormal record became slightly more abnormal. However, none of the abnormalities seen was of a specific variety and all consisted of bilateral or generalized episodic, usually rhythmic, and synchronous four to six per second waves with an amplitude not exceeding 35 microvolts. In none of the records was there any significant change of the alpha frequency, response to hyperventilation, or the response to photic stimulation after reserpine medication.

In an additional 15 patients, electroencephalograms were recorded after at least six weeks of reserpine therapy consisting of an average of 1 mg. total daily dosage. This group consisted of nine females and six males ranging in age from 27 to 56. Of these, 11 were normal, three showed minimal nonspecific abnormalities, and one showed a rather

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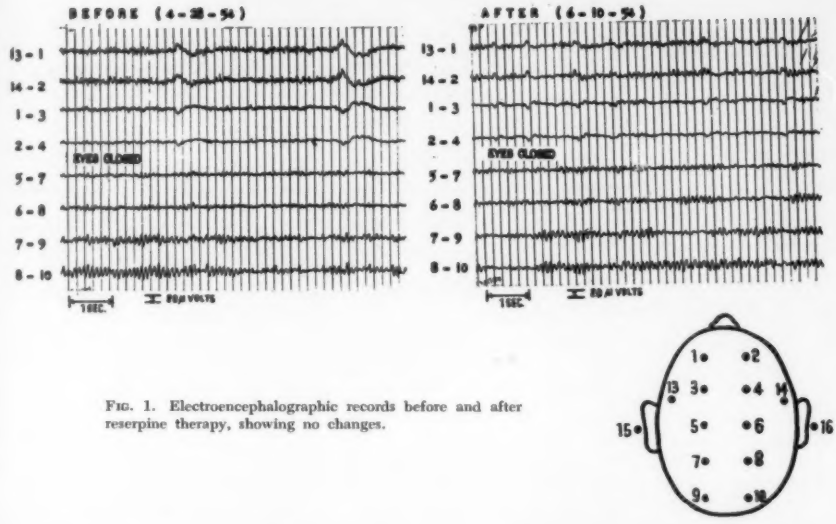

FIG. 1. Electroencephalographic records before and after reserpine therapy, showing no changes.

marked focal asymmetry with slowing in the right occipital region. No consistent feature was seen in these records to suggest that they were affected by reserpine. Inasmuch as the patients recorded were hypertensives, it would seem more logical to assume that the minor changes seen in the electroencephalographic records were secondary to hypertension or other vascular changes rather than to the drug. It is interesting to speculate that the two records which reverted to normal following reserpine therapy were the results of the beneficial effect of reserpine, acting secondarily through its effect on hypertension.

It has been inferred[1,2] that reserpine must act differently from the barbiturates since there are different effects on the electroencephalogram. This inference was apparently based on the observation that intravenous barbiturates induce sleep and accordingly electroencephalographic changes, whereas intravenous reserpine had a more delayed action and did not actually cause sleep, but only allowed it when the animal was undisturbed, at which times electroencephalographic changes of sleep could be expected.

When barbiturates are given orally, there is little, if any, change in the electroencephalogram in the majority of subjects.[3] Therefore, since we found no change in the electroencephalogram after oral reserpine, one could conclude that reserpine and barbiturates had similar modes and sites of action. Obviously, either conclusion is spurious and the changes or lack of changes in the electroencephalograms of either animals or humans thus far observed cannot be used to decide where or how the drug acts. It is of greater value to observe the clinical effects of these drugs and draw conclusions therefrom.

SUMMARY

No consistent effect from reserpine could be detected in the electroenceph-

alograms of 26 humans. In 11 of these, comparisons could be made to the electroencephalograms prior to the reserpine therapy. The information gathered gives no positive clue as to the mode or site of action of reserpine or its differences or similarities to barbiturates.

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2. *A propensity to bend the trunk forwards, and to pass from a walking to a running pace.* This affection, which observation seems to authorise the being considered as a symptom peculiar to this disease, has been mentioned by a few nosologists: it appears to have been first noticed by Gaubius, who says "Cases occur in which the muscles duly excited into action by the impulse of the will, do then, with an unbidden agility, and with an impetus not to be repressed, accelerate their motion, and run before the unwilling mind. It is a frequent fault of the muscles belonging to speech, nor yet of these alone: I have seen one who was able to run but not to walk."

James Parkinson in *An Essay on the Shaking Palsy,* published in 1817.

CLINICAL PATHOLOGIC CONFERENCE

Raymond D. Adams, M.D. Section Editor
with the assistance of E. P. Richardson, Jr., M.D.

Presented by *Charles D. Aring, M.D.*

CASE PRESENTATION

A 12 and a half year old white girl was admitted to the hospital on March 21. She had been well until some 12 days prior to admission, when she began to complain of throbbing headaches over the right eye. They had persisted and were associated with anorexia, decreasing activity of bowels and bladder, and lethargy. She had been seen by a physician some eight days before admission who said she had sinus trouble and treated her with a pinkish-orange medication. One day later she began to vomit and vomited everything that she ate for the ensuing week. Occasionally there was vomiting without ingestion of anything. The vomitus was described as foamy and green. She had not had a bowel movement for a week and an enema was administered on March 21. The parents said that she acted dizzy and weak but otherwise was all right. She had not had any fever up until March 21. She had been warm and perspired profusely. She walked about in the early morning of March 21, but refused to stand thereafter. She is said to have been well oriented during the period before coming to the hospital.

A review of her developmental and past history revealed that she was delivered at full term, weighing 9¾ pounds at birth. She was said to have sat up at six months, walked at 15 months, and talked at two and a half years. She had achieved the fourth grade of school only by reason of age and not by ability. The parents felt that she was much slower than their three other younger children. The mother had not realized that the child was retarded until after she started school; the patient had gone to school only because she was required to do so. She was described as being usually quite withdrawn, but she sometimes played with other children in the neighborhood. The report from the school corroborated most of this, and their opinion was that other children were fond of her and that she was not a behavior problem. The family physician said that she had had measles, chickenpox, and pertussis without apparent complications. A tonsillectomy had been done at the age of six years.

Her family physician said that he had treated the father for a stomach ulcer for a number of years and considered him to be neurotic and a worrier, that the mother was the more intelligent of the two, and that both seemed fond of the children. The mother was said to have been ill quite a bit during the past few years; she had had several miscarriages. The mother was Rh negative and the youngest child had required exchange transfusion.

Examination on March 21 revealed a blood pressure of 80/50, temperature 96° F. orally, pulse 82, and respirations 18. The child was fairly well developed but emaciated; she appeared both acutely and chronically ill. Her skin was pale and dry and there were no eruptions. The abdomen was scaphoid, and there was tenderness in the right upper quadrant. The lungs were clear to percussion and auscultation; the heart was not enlarged; there was a grade 2 systolic murmur presumably at the apex. There was 1 plus nuchal rigidity; neither

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Kernig nor Brudzinski signs were elicited. The reflexes were all recorded as normal. The pupils were equal and reacted well; the optic fundi were normal. One examiner noted "she became hysterical when asked to stand, collapses when made to stand, and objects to sitting." She was given intravenous fluids. She was noted to be irritable, crying frequently for her mother.

For the first few days she refused even small quantities of fluids by mouth. Her weight was recorded as 45½ pounds on March 23. On March 22 the resident physician noted that the child objected violently to intravenous drips, and it was decided to attempt to do without them. She remained miserable, but her only specific complaint was pain over the right eye. During the first two days in the hospital the temperature was around 99° F. On March 24 the resident noted that she was afebrile; another examination added nothing. He felt that the patient was a dull child for her age, cried a great deal, and wished only to be left alone. On the subsequent days, the nurses' notes indicate that she took oral nourishment and slept a great deal.

On March 24 she again began to refuse all food and complained of feeling sick. She took only a small amount of liquid. On the morning of March 26 she again refused food. She was described by the nurses as being lethargic and she complained of headache, refusing even to brush her teeth. That same morning she did not want her bath, only wanting to be left alone. Shortly after the bath, she had her first episode of vomiting since coming to the hospital on March 21. She was described as lying very still without moving even when expectorating. She was put on a cart and asked if she wished to watch television. She showed no interest and fell asleep shortly after being taken to the television room. She continued to refuse her diet, slept most of the day; however, at the time of the evening meal, the mother was able to coax her into taking a small amount of food, which the child promptly vomited. She refused the evening nourishment and when asked what she would like, she refused to answer and went to sleep immediately. Frequent notes of refusal of food and lethargy continued and only rarely did she not vomit. Her weight was 44¾ pounds. A resident physician noted that they had considered discharging her because of her inability to relate to anybody on the ward.

On March 29 she awoke shortly after midnight and threw up a large amount of whitish-yellow vomitus. She would not move from the saturated bed without help, cried, and seemed quite irritable. It was noted that she did not want to sit up because she got dizzy. She was described as being withdrawn and uncooperative. She continued to vomit, lying in her vomitus. Later in the morning, while listening to the phonograph in the playroom she fell asleep repeatedly. She refused to talk and constantly lay on her left side. In the afternoon she complained that her left ear hurt. On the morning of March 30 she took some water eagerly and vomited it immediately. The notes on that day recorded an increase in the deep reflexes in the left leg over those in the right; otherwise as much of a routine neurologic examination as could be done on an uncooperative, reclining patient was normal. She seemed very irritable and required intravenous fluids; she took small amounts of fluids by mouth, cried, moaned, and complained of headache. Her weight was 43 pounds. She refused to talk to the resident physician when he came to see her at eight o'clock that evening. At 8 p.m. March 30 the blood pressure was 100/74. At 9 p.m. while a house officer was working with her, she abruptly became comatose and ceased breathing. Caffeine failed to produce any response. The blood pressure was unobtainable; a laryngoscope was passed and dried secretions were found in the throat; the airway was not considered to be obstructed. Nevertheless tracheotomy was performed and she was placed in a respirator. At this time, her right pupil was noted to be dilated, the left constricted; shortly both pupils became dilated and did not react. She was seen by neurosurgical consultants, who found her to be completely flaccid and areflexic. There was no abnormality in the optic fundi. The child remained in a respirator, never responding again. The nurses noted that she occasionally moved the right extremities but not the left during the two days in the respirator.

Hemograms on March 22 revealed 12 gm. of hemoglobin, adequate platelets, 8,000 white blood cells, 84 per cent neutrophils; on March 25, hemoglobin was 13.7 gm. Sedimentation rate was 17 on March 25. Routine urine examination was normal; urine specimens of March 30 and 31 contained albumin, sugar, and acetone. A good deal of blood chemical study gave no indication of metabolic abnormality.

Two lumbar punctures were performed, the first on March 21 revealed an initial pressure of 130 mm. of water with good relaxation; the fluid was clear and contained no cells; total protein was 12 mg. per cent, sugar 85 mg. per cent, and chlorides 120 mEq/L. Cultures were negative. The second lumbar puncture was performed in the respirator shortly after her collapse. This revealed an initial pressure of 210 mm. with a respirator cuff about the neck; only 0.5 cc. of fluid was removed which

was water clear; six red cells per cu. mm. were counted; the sugar determination was 113 mg. per cent.

The vital signs were as follows:

Date		Temperature	Pulse	Respirations	Blood Pressure
3/21		96 (O)	82	18	80/50
3/22		99.4	72	16	124/100
3/23	8 a.m.	98.6	96	20	104/88
	8 p.m.	98	68	16	96/70
3/24		98	80	20	98/68
3/25	7 a.m.	97	92	20	118/92
	8 p.m.				120/100
3/26	8 a.m.	98.6	126	22	108/78
	8 p.m.	99 (R)	80	12	110/98
3/27		99	98	16	104/92
3/28		98	60	16	100/80
3/29		98	100	20	104/84
3/30	8 a.m.	99	88	22	100/80
	8 p.m.				100/74

Roentgen pictures of the sinuses were normal on March 22. A chest film revealed pulmonary calcification, and the question of tuberculosis and histoplasmosis was raised. Skull films taken on March 25 were interpreted as normal. Repeated skull films on March 31 raised a question as to the significance of a small calcification which had previously been considered artifact. The calcification was in the region of either the pineal gland or choroid plexus. The radiologist pointed out that calcification in these areas is unusual in childhood.

PPD B test was negative; histoplasma 1-100 was reported as 2 plus.

DIFFERENTIAL DIAGNOSIS

DR. MILTON ROSENBAUM (professor of psychiatry and attending neurologist): The essential points in the history were that this 12 and a half year old girl was suffering from acute symptoms of only about 12 days' duration; these were headache over the right eye, vomiting, lethargy, dizziness, and generalized weakness. It is interesting to note that she was up and about until the day of admission to the hospital, and then for some reason or other she did not want to stand or walk. I would consider the past medical history essentially normal except for the obvious mental retardation.

The physical and neurologic examinations were essentially normal except for emaciation, but the child appeared to be both acutely and chronically ill. The only other sign of note was slight stiffness of the neck. One examiner noted that the patient "became hysterical when asked to stand, collapses when made to stand, and objects to sitting." I will have something to say about this later. The behavior of the patient did not seem unusual to me. That a 12 and a half year old child, who was mentally retarded and had been well protected by her parents, became quite fearful and apprehensive and cried for her mother on being confined to the strangeness of a hospital is not an indication of abnormal behavior. The laboratory work including cerebrospinal fluid examination was essentially negative. The urinary findings reflected the general dehydration and malnutrition resulting from the vomiting.

Now what were the diagnostic possibilities at that time? From the thorough workup, it would seem to me that in the initial phase the ward doctors suspected some type of central nervous system disease, most likely meningitis, probably tuberculous, or a brain tumor. However, the normal findings on physical, neurologic, and laboratory examinations, and especially the normal cerebrospinal fluid and skull roentgenograms, did not support a diagnosis of central nervous system disease. I would guess that within a few days after she was admitted a diagnosis of a functional disorder, probably of neurosis, was made. This diagnosis then led to the detailed social history, parts of which are summarized in the protocol. I would interpret the excellent family and social history as revealing that this child was mentally retarded but was making a fairly good adjustment. She was somewhat withdrawn, apparently could not keep up with the other children, and was pushed somewhat by being placed in the fourth grade, but I would not consider her behavior to be too abnormal. It seemed to me that the relationship to the parents was essentially good.

Now, what about the attitudes of the physicians toward the patient? I am sure that many of us have also been in situations where somehow we missed a diagnosis. Then out of our frustration and the

blow to our self-esteem, we unfortunately made a diagnosis of a neurosis on the basis of negative physical and laboratory findings rather than on the basis of positive findings of a neurotic disorder, and in the process became a bit hostile to the patient. There are a few clues in the protocol concerning the attitude of the doctors to the patient, for instance, the previously mentioned statement that the patient became hysterical when asked to stand. Now what does that mean? Does it mean that the patient showed "la belle indifférence," or does it mean that the patient was apprehensive, frightened, and excited? If a lay person used the term "hysterical" to describe behavior, I could understand, but as doctors we should not use terms which reflect value judgments. To me the word "hysterical" used in such a setting represents a value judgment rather than a description of behavior. The word "hysterical" was equivalent to saying "she's a little brat;" and actually later on, there was a statement to the effect of "What is she doing here anyway; she ought to be sent home." It is easy for us to fall into such an error. We are only human, but I believe that as doctors we have to rise above our human frailties in order to perform our task, and therefore we must at least try to prevent our own anger and other personal emotional feelings from interfering in our relationships to our patients. I think it is perfectly obvious that what happened in this case was that the frustration resulting from the inability to make the diagnosis led to the development of negative counter-transference attitudes on the part of the physicians.

To me, the fact that this little girl refused to stand or even to sit up was a most important clinical finding and it was overlooked. I believe that the child refused to stand or sit because of some disturbance in her central nervous system, especially in those areas that have to do with trunk equilibrium, probably the cerebellum. However, the symptom was interpreted as a behavioral sign in a negative way. The complaint of severe headaches over one eye, quite unusual in a child, together with lethargy, dizziness, and the specific inability to stand or sit points to a lesion in the posterior fossa. Against this was the normal cerebrospinal fluid and the normal optic disks, because of which the general picture of a very sick child was overlooked.

The child, although afebrile and without any particularly new physical or neurologic findings, remained lethargic, cried, and wanted to be left alone. As I have already mentioned, the frustration of the house staff in dealing with her became quite obvious, and despite the onset of vomiting and increasing drowsiness, she was considered for discharge because she was not relating to anybody on the ward. She was described as withdrawn and uncooperative. Again I think this description is a value judgment; my guess is that if a diagnosis of brain tumor had been made at that time, she would not have been called uncooperative and the house staff would have had no difficulty in dealing with her. Although this is my own interpretation, I believe that the heroic efforts made to save this girl before she died resulted in part from the change in the physician's attitude toward the patient once it became obvious that she was seriously ill physically.

Now what about the differential diagnosis? It is safe to say that the patient had central nervous system disease. The history, as already indicated, points to a brain tumor. However, such symptoms as drowsiness, vomiting, lethargy, and headache do not help to localize the tumor. Now what are the localizing signs in this case? First the frequency of cerebellar tumors in children would make me suspect that location immediately. The vomiting was an interesting symptom in this case. We usually consider vomiting in brain tumor patients to be a manifestation of increased intracranial pressure, but in this case we have no evidence of increased intracranial pressure either in the optic disks, the spinal puncture, or skull films. Therefore, I would sus-

pect that the vomiting in this instance was due to direct involvement or pressure on the lower brainstem, on medullary centers that have to do with vomiting. Therefore, her vomiting would also point to a posterior fossa localization. The headaches over the right eye have some localizing value because they are an indication of disturbance in the function of the fifth cranial nerve. We know that this is not uncommon in posterior fossa lesions in which there may be stretching of the tentorium, which is supplied by the fifth nerve.

However, the most important localizing symptoms and signs and those that I lean on most heavily in my diagnosis are the subjective complaints of dizziness, refusal to sit or stand up, and the desire to lie quietly in bed without moving. These latter symptoms I would consider defensive but not against instinctual impulses. If they were defenses against instinctive impulses, then I would say that they were hysterical symptoms. I believe these were defensive symptoms to protect the patient from experiencing the pain and suffering of cerebellar dysfunction such as dizziness, vertigo, and truncal ataxia. Any of you who have seen patients suffering from acute labyrinthitis or an attack of Menière's disease know that they want to lie quietly; they are relatively comfortable if you allow them to remain flat in bed, but when they move their head a little to one side or another, they become sick, vomit, and may go into collapse. So we let them lie quietly in bed without moving to protect them from such suffering.

The final episode is clearly that of a medullary death, and again this would point to a lesion in the posterior fossa. A word about the possible cause of the final episode. As you know, the final episode was very sudden, dramatic, and catastrophic in its onset. Such episodes in neurologic cases usually point to a vascular lesion. I believe that she did have a vascular lesion in the medulla; probably the blood supply of the medulla was embarrassed as a result of venous engorgement, due to pressure or direct involvement by a tumor, or possibly by sudden herniation of the medulla into the foramen magnum.

How do we explain the lack of increased intracranial pressure? I really do not know the answer, but it obviously means that there was no interference with ventricular circulation, that is, there was no internal hydrocephalus, and that this lesion was fatal not because of its size but rather because of its particular location. Then, of course, if she had had increased intracranial pressure and choked disks, I would not be here to discuss this case; it would have been too simple. If every patient followed the text books, we could prune medical school work down to about one year, but then medicine would not be much fun. So here we have a patient who probably had a cerebellar tumor and yet did not show signs of increased intracranial pressure. The slightly elevated sugar in the cerebrospinal fluid is without significance, and is well within the range of sugar values in brain tumors as reported by Merritt; the elevation in our case was probably due to the intravenous glucose which she had received.

I believe the main differential diagnosis to be between a midline cerebellar tumor, probably a medulloblastoma, and a fourth ventricle tumor. Both could have produced this patient's clinical picture. However, I believe the normal cerebrospinal fluid findings, especially the normal protein, and the lack of other signs of increased intracranial pressure are against the diagnosis of a fourth ventricle tumor. Therefore, I would make a diagnosis of a midline cerebellar tumor, a medulloblastoma. In favor of this latter diagnosis, I would list the following: the frequency of this type of tumor in young children; the rapid course; the vomiting in the absence of increased intracranial pressure, which probably means direct pressure on the vital centers in the brainstem; and the important signs of dizziness and inability to stand and walk despite good functioning of the extremities when the patient

was examined in bed. The latter brings up an important point often overlooked in clinical neurology, that is, the necessity to examine the motor system of every patient by having them stand and walk if it is at all possible to do so. When we examine patients in a hospital, they are usually in bed and classically they are examined in that position. I have seen patients who reveal no neurologic defect when examined in bed, but when the patient is asked to walk, slight weakness of an extremity becomes evident. Here we have known intimately the experience of missing cerebellar lesions – tumors and intracerebellar hemorrhages – because the patient was examined only while reclining. The midline cerebellar regions have to do with maintaining equilibrium in the trunk and extremities during standing and walking rather than with the functioning of individual muscles or individual extremities. Midline cerebellar lesions characteristically manifest themselves with truncal ataxia, and cerebellar control of the extremities may be normal in such lesions.

DR. CHARLES D. ARING: In their written discussions, 19 of the students believed the trouble to be caused by a tumor; ten of these 19 thought that it was an ependymoma of the fourth ventricle, six that it was a medulloblastoma (midline), and three that it was a glioma of the third ventricle. Seven thought that an infection was operating; of these seven, one believed it to be a virus encephalitis, one a thrombosis of sigmoid and superior longitudinal sinuses secondary to left middle ear infection and malnutrition, and five an abscess. Three localized a frontal abscess, one believed that abscesses were multiple, and one said that the abscess was subtentorial but didn't localize it further. Four of the students made a diagnosis of subdural hematoma over the right convexity.

As you can imagine the service diagnosis varied from time to time. In the admission diagnosis on March 21, the following impressions were recorded: 1) Vomiting of unknown cause; rule out hepatitis, gastroenteric, and genitourinary causes. 2) Since the cerebrospinal fluid is normal, I now doubt tumor or meningitis. On March 27 the following diagnostic speculation was entered in the record: "I do not believe we are going to find a specific physical process to explain this child's problem. She is without doubt retarded, but there is a severe emotional problem involved here." Then the final diagnosis at the time of death was, 1) Mental and physical retardation; 2) pulmonary histoplasmosis, inactive; 3) intracranial tumor; possibly ependymoma of third ventricle.

The written discussions by the students were generally quite thoughtful. I have no specific advice or criticism; perhaps some of you worried a bit too much about the cerebrospinal fluid sugar values; you must know that patients who are vomiting or who are in coma usually are given intravenous fluids and that some of these fluids are apt to contain glucose. This will reflect itself in the cerebrospinal fluid if a tap is done in proper temporal relationship to the intravenous injection. Several of you discussed thoroughly and straightforwardly the counter-transference problems much as Dr. Rosenbaum discussed them; some of you didn't mention them, perhaps believing that neurologists are interested in more structured things. One doesn't abrogate one's function as a physician on becoming a neurologist.

The case is open for discussion.

DR. DANIEL OSHER: I agreed with most of what Dr. Rosenbaum has said; his diagnosis is probably about right. In my personal experience, I have never seen a medulloblastoma without papilledema. Another point that makes one lean a bit more to the possibility of a ventricular tumor was the patient's reluctance to turn or indeed to move. These patients with less room in the caudal portion of the ventricular system have a prejudiced equilibrium, to put it mildly. I was going to ask a question about the roentgenograms.

DR. ARING: Our roentgenologist has not made his appearance, so I will substitute for him. I do not believe that the small calcification, which I would place in the choroid plexus in both skull films, is significant. I think it falls into the feverish activity that Dr. Rosenbaum remarked on after this girl went into coma. The previous skull films were re-examined and they then took another series, and I believe they were straining at the bit in their interpretations.

DR. FRANK F. ESPEY: I wonder whether or not an electroencephalogram would be expected to show changes in the occipital leads, as a sort of neighborhood effect?

DR. SAMUEL A. TRUFANT: Unless there was a lesion large enough to involve cerebrospinal fluid pathways, it would be more likely to show frontal slowing because of frontocerebellar connections. Those that show occipital abnormalities are more likely to be in one cerebellar hemisphere pushing up on the undersurface of the tentorium; this effect would probably be via some vascular embarrassment rather than directly due to pressure because the tentorium is a rigid fibrous structure. Another point in considering the electroencephalogram is that most patients who have increased intracranial pressure show diffuse slow dysrhythmia as a secondary effect.

DR. OSHER: I was wondering what I would have done further to pursue the diagnosis, had I seen this patient and suspected a posterior fossa lesion. Would one do an air study or should one go ahead with posterior fossa exploration?

DR. ESPEY: I think you'd probably screw up your courage after watching her for a week or so and do a ventriculogram and apologize to everybody for the needless procedure. A ventriculogram may well have been normal in this instance.

DR. ARING: Dr. Landing, will you enlighten us?

PATHOLOGIC DISCUSSION

DR. BENJAMIN LANDING (assistant professor of pathology and pediatrics): I can preface this by saying that except for the fact that we didn't have to cope with counter-transference phenomena, we had as much difficulty in arriving at an answer as some of the people who saw her while she was alive; our initial thoughts on the nature of the disease were no more correct than those of some of the clinicians.

At autopsy she was poorly nourished but reasonably well-developed. The only striking findings visible externally were asymmetric pupils; the right pupil was 6 mm. and the left 9 mm. Her lungs were large and boggy; the spleen was unusually small, less than half the normal weight, but showed no scars or areas suggestive of tuberculosis or histoplasmosis; and her kidneys, which we can probably take as an indication of her general developmental and nutritional state, were distinctly small with a combined weight of 113 gm. Normal for her age would be 193 gm., so she was well below normal development. Microscopically, the lungs showed edema, early bronchopneumonia, and purulent bronchitis. No evidence of histoplasmosis was found.

Her skull was unusually thick and when the dura was opened, the brain was seen to be of normal size; the gyri appeared relatively flat and the sulci narrow as if she had cerebral edema, and this was confirmed microscopically. The brain was within 1 gm. of normal weight by the standard table, weighing 1,350 gm. This makes us feel that it may well have been somewhat small before the terminal episode because grossly and also microscopically it appeared edematous.

When we removed the cerebellum, the right cerebellar hemisphere ruptured and about an ounce of creamy material came out, which we thought grossly was pus. A culture of this grew *E. coli* subsequently. We had thought at autopsy that we had the answer in a cerebellar abscess.

When the fixed brain was cut, a cavity was found in the cerebellum which did not communicate with the ventricles or, before evisceration, with the meninges (figure 1).

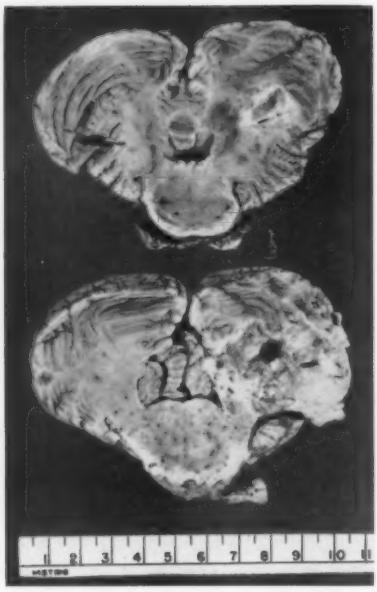


FIG. 1. Vertical sections of the cerebellum and brainstem at the level of the pons to show the lesion, mainly in the white matter of the right cerebellar hemisphere. The congestion is also seen in this photograph, particularly in the pons.

You can see the large cavity lined with shaggy friable, yellowish material. As far as we can tell, the contents before evisceration had been thick, creamy material with no fluid of lesser consistency. The margins are a little difficult to make out and exactly how it graded into the surrounding tissue was not to be easily definable by palpation. Another gross finding which caused difficulty, and of which we do not have a photograph, was a yellowish-gray, rather soft membrane which lined the lateral ventricles. We had thought grossly that this represented evidence of ventriculitis or ependymitis.

The microscopic preparations showed a broad band of gliosis lining the lateral ventricle and no true ependymal cells. There were little ependymal nests deep in the layer where the terminal veins lie; it is our interpretation that this layer was ependymal scar or ependymal gliosis. There was no obvious evidence of inflammation, and I am not sure what we should consider to be the cause of this lesion; whether this is the result of old inflammation or of old intraventricular hemorrhage, I don't know. At any rate this lining of the lateral ventricles appears unrelated to the cerebellar lesion.

The cavity in the right cerebellar hemisphere lined by quite cellular tissue was extensively necrotic. In a high power study, these cells tended to be rather elongated or banana-shaped, but occasionally one saw a small whorl or a "cell within a cell" appearance. Our microscopic studies have been extensive, trying to determine whether this should be considered phagocytosis or whether this is a minimum degree of whorling which meningiomas can show. The line between the cellular tissue and the adjoining cerebellar tissues is reasonably sharp in some areas and in others rather poor, and with phosphotungstic acid hematoxylin stain one can see residual axons running through the border where this tissue is merging with the adjoining cerebellum. I am not sure whether this should be considered invasion or simply poor demarcation.

DR. OSHER: Did you see any giant cells?

DR. LANDING: There is some variation in cell size and shape and nuclear size and shape, but I think no true giant cells; it isn't the standard glioblastoma multiforme or astrocytoma grade 3 or 4. The abnormal cells all seemed to be of the same type even in necrotic areas. The cell type had clear-cut cytoplasmic borders. No glial fibrils were identified with phosphotungstic acid stain, and reticulin stains were also unrevealing.

Along the borders of this pathologic tissue where it joined the more normal cerebellum, intermingling with the white matter was seen. The tumor cells ran into the affected white matter with no very sharp demarcation.

These microscopic findings came as a surprise to us because we had thought grossly that the cerebellar lesion was an abscess and that the ventricular lesion was ependymitis; however, the lesion seems quite clearly to be neoplasm. I've had difficulty in deciding whether or not it is a malignant neoplasm. I'm not sure that the patient died because of rapid or extensive growth of this tumor as opposed to sudden necrosis with medullary compression, and we would agree that the sudden collapse and respiratory arrest were the result of medullary compression; petechial hemorrhages were found in the brainstem. If you simply take it as a cystic tumor of the cerebellum with rather poor demarcation from the surrounding tissue – in fact an intermingling of the border of the tumor with the adjoining tissues – that fits the description of a low-grade astrocytoma, and one might choose to call this a polar spongioblastoma, which is an old term for a variant of rather low-grade astrocytoma with rather elongated cells. They don't, as far as I know, classically occur in this region, but I think this may be the correct interpretation. The alternative, I think, is to go far the other way and say that this is an extremely malignant, undifferentiated glioma. I think the slight evidence of whorling and "cell within a cell" effect is not enough to make me feel that this was either a microglioma or a meningioma, and I favor the opinion that this was actually an extremely malignant, undifferentiated glioma, probably in the astrocytoma series. Dr. Dorothy Russell of London, who went over these slides with us, believes that the tumor was a medulloblastoma differentiating to form spongioblastoma. I think the possibility that it was actually not a very malignant astrocytoma, but one which just happened to drift toward polar spongioblastoma in having elongation of the cells, is a very real one, however.

One additional finding which I forgot to mention is that this patient had almost total ischemic necrosis of her pituitary gland, a sort of a Simmonds' disease-like pituitary necrosis, which we would relate to her general vascular collapse.

CLINICAL DIAGNOSIS

Intracranial tumor, possibly ependymoma of the third ventricle.
Mental and physical retardation.
Pulmonary histoplasmosis, inactive.

DR. ROSENBAUM'S DIAGNOSIS

Medulloblastoma of the cerebellum causing medullary compression.

PATHOLOGIC DIAGNOSIS

Glioma of the right cerebellar hemisphere.
Congestion, edema and petechial hemorrhage of the brain.
Ischemic necrosis of the pituitary gland.
Bronchopneumonia.
Purulent bronchitis.
Physical retardation.

DR. OSHER: Young neurosurgeons may be fooled by the appearance of this process on opening into a tumor and obtaining what looks like pus. Almost invariably such a tumor turns out to be either a metastatic carcinoma or a very malignant type of glioma. The slower growing ones form cysts; at least I've never seen one that formed material such as you've described. I think this is a strong point in favor of this lesion being a variant of a malignant glioma.

DR. ARING: Were there any evidences of pressure about the brain, Dr. Landing?

DR. LANDING: There were none. I don't know that there might not have been two days before. There was tremendous congestion, edema, and scattered petechial hemorrhage throughout the central nervous system.

DR. J. PARK BIEHL: Were there polymorphonuclear leukocytes present?

DR. LANDING: No, there was no significant inflammation; I think it was just necrotic tumor.

DR. JOHN CAMPBELL: Perhaps I should be, but I'm not familiar with the term, microglioma; do you mean oligodendroglioma?

DR. LANDING: It is essentially reticulum cell sarcoma. Russell and others have described solitary tumors of the brain of that type and said they must be tumors of the microglia.

DR. ARING: At this point, would any of the neurosurgeons like to tell us what he might have done in the way of further diagnostic maneuvers?

DR. OSHER: Well, I have already noted my own personal quandary. I think I would have been tempted to watch this girl because she had none of the usual localizing signs and she had no signs of increased intracranial pressure. She was being watched, and as it turned out, she developed this brainstem syndrome and died. In retrospect, I think with this probably very malignant tumor, the chances of removal or cure would have been slim. Yet I think there is no doubt that if we had operated correctly, she wouldn't have had this catastrophe. I think this tumor could have been removed or she could have been decompressed and given x-ray therapy; I doubt if she could have been cured.

DR. ROSENBAUM: I still don't like the implication that there weren't any positive findings. After all she had headache over the right eye; she couldn't stand, couldn't walk, complained of dizziness; she didn't want to sit up and in fact couldn't move. Correctly interpreted, these are all localizing signs; there still is something to clinical neurology.

DR. OSHER: If we had gotten to this case before she went into this last state, a ventriculogram would have been normal.

DR. ARING: And so likewise probably a vertebral angiogram.

DR. BIEHL: Can the mental retardation be associated with the gliosis in the ependyma?

DR. LANDING: I think very possibly, in that both are consequences of some earlier brain disease, the nature of which I am not sure; it might have been infection or birth injury with hemorrhage. We have great difficulty in judging the state of the cerebrum in many patients with mental defect; as a matter of fact, many of them have grossly and microscopically normal cerebrums. Even patients with frank cerebral palsy may have grossly and microscopically normal cerebrums. It is sometimes said that they have a diffuse decrease in ganglion cells, but you probably don't recognize a 10 per cent decrease in ganglion cells.

DR. OSHER: Did the cortical sections show anything striking?

DR. LANDING: No.

DR. ESPEY: Was the cerebellar lesion close to the surface? You mentioned that what you thought was pus flowed when you removed the contents of the posterior fossa. Were there any surface manifestations at all on the cerebellum?

DR. LANDING: I don't know, perhaps if one looked critically enough. I did not notice anything on the surface before the thing ruptured while we were removing the contents of the posterior fossa.

DR. ESPEY: The contained lesion may be the reason for the normal cerebrospinal fluid protein. I was wondering, even if the protein had been elevated whether one would have entertained the possibility of an abscess.

DR. LANDING: The case was even more remarkable when we thought it was an abscess.

DR. ARING: When the pathologist is confused, you know the case is difficult. It seems to me that a neurologist or neurosurgeon of the old school may have made the diagnosis at the bedside in this case. It appears that air studies and angiograms would not have proved helpful, and quite obviously the normal cerebrospinal fluid threw everybody off the track. Without the benefit of the laboratory, the older clinician had to rely on the history and the examination. As Dr. Rosenbaum has already demonstrated, an answer was to be had in this case only by concentration on these factors.

CASE REPORT

Osteogenic Sarcoma of the Tibia Metastatic to the Brain

Arthur Arnold, M.D.

INTRACEREBRAL METASTASIS of sarcomatous lesions in general and particularly of sarcomas of bony origin are extremely rare in occurrence, whereas primary sarcomas of the brain[1–3] are much more frequently observed. Reports of metastasis to the brain of a leiomyosarcoma,[4] melanoblastoma,[5] lymphosarcoma,[6] and myoblastoma[7] have appeared in the literature, but only a single case of osteogenic sarcoma metastatic to the cerebral hemispheres has been previously reported. Harding and Courville[8] reported a case of a Mexican laborer with a primary lesion in the left femur, in whom x-ray films of the skull revealed a calcified mass in the right occipital region. At autopsy a hard bony tumor measuring 4.2 by 3.8 by 2.7 cm. was found in the right occipital cortex. Other smaller lesions containing calcareous material were found in the left precentral and postcentral convolutions.

The present case is unusual in that 21 months after the primary lesion was first detected in the left tibia, the patient began to complain of headaches, and films of the skull revealed a huge, single calcified metastasis in the left occipitoparietal cortex. At autopsy the lesion was found to be entirely intracerebral and caused compression and destruction of the brain. The lesion was bony-hard and had to be cut with a saw.

CASE HISTORY

A 17 year old white male was first seen in the orthopedic outpatient service of the University of Illinois, complaining of enlargement of the left leg just below the knee which was painful only on weight-bearing. Four weeks prior to his first visit to the clinic, the patient was kicked by a bull just below the left knee, following which he developed a small black and blue swelling. A week later, a roll of baling wire injured the same area of the left leg and thereafter the swelling became progressively larger. The patient was admitted to the hospital and a diagnosis of osteogenic sarcoma of the proximal one-fourth of the left tibia was made by roentgenographic examination, and a mid-thigh amputation was performed. Microscopic examination of the tumor confirmed the clinical impression. The patient was fitted with a prosthesis and discharged to his home.

From the department of neurology and neurological surgery, University of Illinois at the Neuropsychiatric Institute, Chicago.

Approximately five months following the left mid-thigh amputation, an area of increased density consistent with a metastasis appeared in the left lower lung field. The patient, however, had no cough or other pulmonary complaints. The operative stump showed no recurrent neoplastic involvement. The number of pulmonary metastases increased during the course of the following year but the patient continued to maintain his weight and felt well. Twenty-one months after detection of the primary lesion, the patient began to complain of occasional severe headaches which were relieved by codein. Skull films were taken and a large, ovoid, calcified intracerebral lesion was observed in the left occipitoparietal region, which was interpreted as a probable metastatic osteogenic sarcoma (figures 1 and 2). Roentgenograms of the skull taken at the time of recognition of the lesion in the leg showed no evidence of metastatic tumor (figure 3). On neurologic examination the patient showed no loss of visual perception and had no visual field defect. The fundi revealed a mild papilledema. The deep tendon reflexes were more active on the right, but no pathologic reflexes were elicited. The patient expired shortly thereafter, 23 months after the appearance of the sarcoma in his leg.

The autopsy findings were: 1) Metastatic lesions to the lungs, spleen, and splenic vein; 2) acute tracheobronchitis; 3) pulmonary emphysema, with patchy atelectasis; 4) hyperemia of the kidneys; 5) atrophy of the heart; 6) acute ileitus; 7) hydropericardium; 8) old well-healed amputation of the left femur without evidence of recurrence.

On gross inspection of the brain a rock-

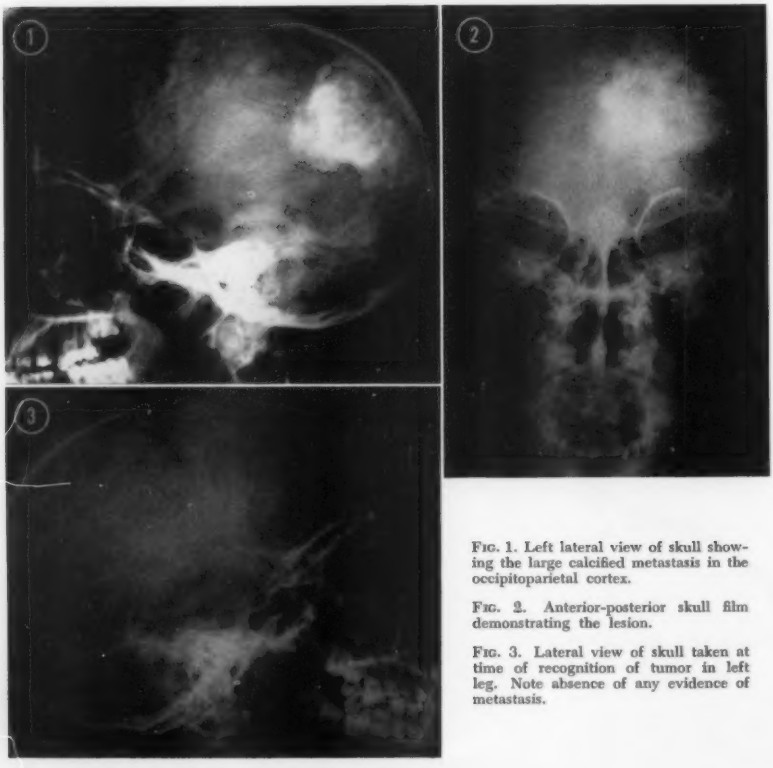
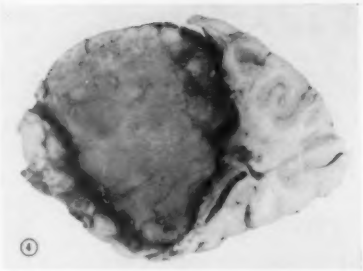


FIG. 1. Left lateral view of skull showing the large calcified metastasis in the occipitoparietal cortex.

FIG. 2. Anterior-posterior skull film demonstrating the lesion.

FIG. 3. Lateral view of skull taken at time of recognition of tumor in left leg. Note absence of any evidence of metastasis.



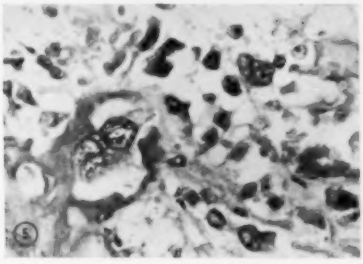


FIG. 4. Metastatic lesion imbedded in parietal cortex. Lateral ventricle displaced laterally and downward.

FIG. 5. Microscopic appearance of the cerebral metastasis which was identical with the primary osteogenic sarcoma of the tibia. Hematoxylin and eosin stain.

hard tumor firmly embedded in the left occipitoparietal cortex was evident. The tumor was loosely attached to the dura mater. The cerebral convolutions were only moderately flattened but marked herniations of the tonsils were noted.

On cross section of the brain the central basal portion of the left hemisphere was softened. The tumor could not be sectioned with a knife; a saw was required. A section of tumor showed a closely trabeculated, porous, bony structure filled with a fatty sanguineous material. The tumor measured 7.5 by 7.0 by 7.0 cm. in its maximum dimensions (figure 4).

On microscopic examination a decalcified preparation revealed a tumor composed of highly pleomorphic, malignant-appearing, oval to stellate cells, lying in a stroma of loose connective tissue and bony trabeculae (figure 5). The cell nuclei varied considerably in size and shape and many cells were multinucleated. Numerous mitotic figures were present. The tumor was similar in microscopic appearance to that of the primary lesion in the left tibia.

SUMMARY

1. In sharp contrast to carcinomas, sarcomas infrequently metastasize to the brain.

2. A case of osteogenic sarcoma, primary in the left tibia, with a huge solitary metastasis to the left occipitoparietal cortex, is reported here.

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CASE REPORT

Postmeningitic Hydrocephalus

Illustrating Dual Origin of the Cerebrospinal Fluid

Harold C. Voris, M.D.

THE ORTHODOX DESCRIPTIONS of the origin, circulation, and absorption of the spinal fluid are well known. They are based on the researches of Weed[8] and the investigations of Dandy[2] and have been confirmed recently by Ingraham and co-workers.[6] The production of internal hydrocephalus with dilatation of the ventricles above the site of a block in either third ventricle, cerebral aqueduct, or fourth ventricle is so commonplace to neurosurgeons that the choroid plexus has in some quarters come to be regarded as the sole source of the cerebrospinal fluid.

Hassin[4] vigorously disagreed with the concept that the cerebrospinal fluid originated in the choroid plexuses, and considered it to be solely derived by drainage from the extracellular fluid spaces of the brain by way of the perivascular spaces into the ventricle and subarachnoid spaces. Instead of its being absorbed into the venous circulation through the arachnoid villi over the convexity of the hemispheres, he believed it escaped from the intracranial and intraspinal subarachnoid space through the perineural spaces of cranial and spinal nerves. He had evolved these views as the result of long and detailed histologic observations on human pathologic material, and he had little patience with the shortcomings of experimental approaches to the problem. Thus, he disregarded certain clinical observations that are commonplace to every neurologic surgeon and denied the role of the choroid plexus in the formation of cerebrospinal fluid. While Hassin did not originate the concept that the cerebrospinal fluid is at least in part derived from the tissue fluids of the brain, he must be given credit for emphasizing the importance of that source and for its demonstration.

The following case report of a child with so-called postmeningitic hydrocephalus illustrates clinically the dual origin of the cerebrospinal fluid.

REPORT OF CASE

A full term female infant was born on August 13, 1952. The anterior fontanelle was smaller than usual but no other abnormalities were noted and she left the hospital with her mother five days later.

From the department of neurologic surgery, Stritch School of Medicine, Loyola University, and the neurologic surgery service, Mercy Hospital, Chicago.

Read before the Chicago Neurological Society, November 10, 1953.

She was readmitted to the pediatric service on April 6, 1953, because of fever, vomiting, and convulsions of three weeks' duration. The rectal temperature was 100° F. There were continuous tonic and clonic movements of the extremities. The neck was stiff and there was mild opisthotonus, bilateral internal strabismus, and a bilateral Babinski response. The circumference of the head was 45 cm., that of the chest 46 cm. Spinal puncture revealed fluid contaminated by erythrocytes. There was no bacterial growth on culture. Bilateral subdural tap was negative. The left lateral ventricle was readily tapped through the anterior fontanelle and appeared to be enlarged. It contained 111 cells, of which 72 were polymorphonuclear leukocytes and 39 were lymphocytes. There was no bacterial growth on cultures of this or any other specimen of spinal or ventricular fluid. A guinea pig was inoculated with the ventricular fluid but never developed any evidence of tuberculosis.

Ventriculography was carried out on April 14, 1953, showing advanced internal hydrocephalus including dilatation of the fourth ventricle (figures 1 and 2). The total protein of the fluid was 470 mg. per cu. mm. The child was thought to have an obstructive hydrocephalus due to inflammatory obliteration of the posterior and basilar cisterns. Ventriculoperitoneal shunt was considered, but was not carried out because of the high protein content of the ventricular fluid and the possibility of tuberculous meningitis. On April 25, 1953 the ventricular fluid showed 53 cells, of which nine were polymorphonuclear leukocytes and 44 were lymphocytes. The total protein was 215 mg. per cu. mm. Opisthotonus was now severe.

A right ventriculoantral anastomosis was decided on and carried out on April 30, 1953, using a modification of the technic described by Nosik.[7] On May 9, 1953 the left ventricle was tapped. The pressure was low and the fluid contained 26 cells, of which three were polymorphonuclear leukocytes and 23 were lymphocytes. The total protein was 200 mg. per cu. mm. The fontanelle remained depressed after the ventriculoantral shunt. Opisthotonus, which had been persistent and severe, gradually improved. Clear fluid drained from the right nostril when the head was lowered.

The child was dimssed on May 28, 1953, but was re-admitted on August 13, 1953. She had been hospitalized at the Municipal Contagious Hospital from June 13 to July 13 for treatment of a bacterial meningitis. At the time of her re-admission the circumference of the head was 46.5 cm. and that of the chest 46 cm. The anterior fontanelle was nearly closed. Clear fluid drained from the right nostril as before when the head was lowered.

Right subdural tap yielded clear fluid. Indigo carmine injected into this space could not be recovered on lumbar puncture. The total protein content of the lumbar fluid was 290 mg. per cc., that of the subdural fluid 173 mg. Injected air proved, on roentgen examination, to be in the subarachnoid spaces, which were dilated. Two days later the right lateral ventricle was tapped at a depth of 6 cm. and ventriculography was carried out. This revealed mildly dilated ventricles much smaller than on April 14, 1953 (figure 3). The total protein content of the ventricular fluid was 13 mg. per cc.

It was apparent that the ventricles were being drained satisfactorily by the ventriculoantral shunt, as indicated by their small size and the normal protein content of the ventricular fluid. The cerebral subarachnoid spaces were enlarged and were not in communication with the ventricles or spinal subarachnoid space, as demonstrated by the various total protein values and the results of the dye test.

Because of the danger of recurrent meningitis it was decided to remove the ventriculoantral communication. It was thought that a ventriculoperitoneal shunt might be attempted if acute ventricular dilatation recurred. The polythene tube connecting the right lateral ventricle with the mastoid antrum was removed on August 6, 1953. The child did well for two days and then expired suddenly after a series of convulsions.

At necropsy a small chronic subdural hematoma was found in the right parietal region. This was only a few millimeters in thickness and did not appear to be the cause of death. The ventricles were markedly dilated in comparison with the recent ventriculogram and there was diffuse fibrous thickening of the leptomeninges, especially in the region of the posterior cistern (figure 4).

DISCUSSION

Discovery of a small chronic subdural hematoma complicated the clinical and pathologic findings in this infant. We can still conclude that the cerebrospinal fluid formed in the ventricles of this infant was drained satisfactorily by the ar-

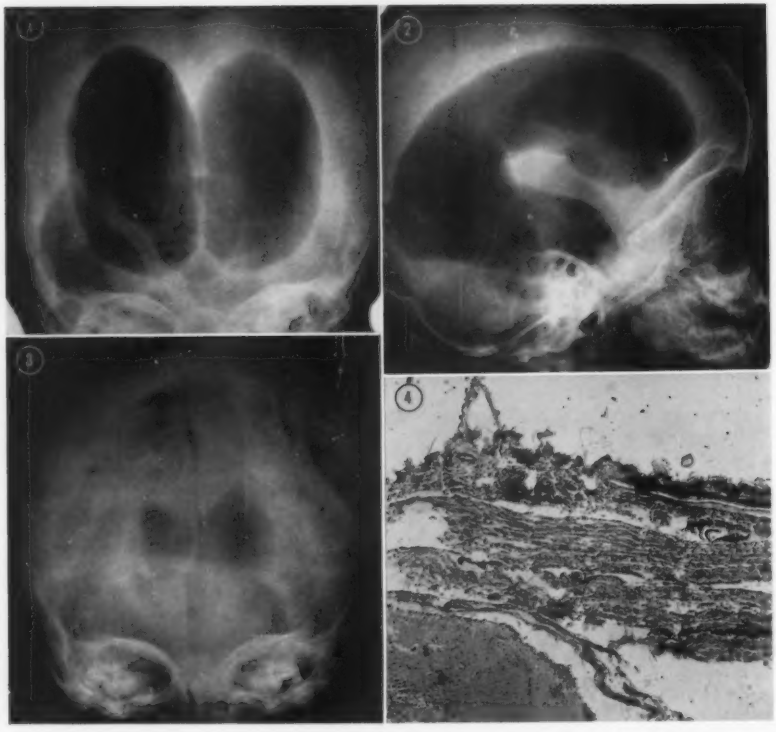

FIG. 1. Preoperative ventriculogram, anteroposterior view. Note greatly enlarged third ventricle.
FIG. 2. Preoperative ventriculogram, lateral view. Note enlargement of third and fourth ventricles.
FIG. 3. Ventriculogram three and one-half months after ventriculoantral shunt, anteroposterior view. Compare with figure 1.
FIG. 4. Microphotograph of leptomeninges in lateral recess of fourth ventricle. Note diffuse fibrous thickening of pia-arachnoid.

tificial shunt between the ventricle and the mastoid antrum. However, there was accumulation of the fluid in the cerebral subarachnoid spaces which were triply blocked, first by inflammatory adhesions between the fourth ventricle and the posterior cistern obstructing the foramen of Magendie and Luschke, second by adhesions blocking the posterior and basilar cisterns from the spinal subarachnoid space, and third by inflammatory blocking of the channels of absorption of the cerebral subarachnoid space into the dural venous channels and the cranial perineural spaces. This accumulation of fluid in the cerebral subarachnoid spaces appears to have been due to drainage of cerebral tissue fluid into the subarachnoid spaces via the perivascular channels.

The tracer studies of Adams[1] with radioactive phosphorus (P^{32}) tend to substantiate the absorption of cerebrospinal fluid from the cerebral subarachnoid space into the dural venous channels. Hassin[5] believed that the perineural

TABLE 1

PROTEIN VALUES OF LUMBAR, SUBARACHNOID, AND VENTRICULAR FLUIDS IN A PATIENT WITH POSTMENINGITIC HYDROCEPHALUS AND ARTIFICIAL DRAINAGE OF VENTRICLE.

Protein value	*Origin of fluid*
290 mg. per cc.	Lumbar subarachnoid space
173 mg. per cc.	Cranial subdural space
13 mg. per cc.	Right ventricle

channels were the most important in absorption of the fluid. Both of these routes were blocked in this patient.

The different protein values of the lumbar subarachnoid fluid, the cerebral subarachnoid fluid, and the ventricular fluid in this case (table 1) are best explained by the dual origin of the cerebrospinal fluid originally suggested by Weed.[8] The fluid appears to be formed from the choroid plexuses of the ventricles by a filtration process and from the tissue fluid of the brain by drainage through the perivascular channels into cerebrospinal fluid spaces. It is absorbed for the most part from the cerebral subarachnoid spaces into the dural venous channels through either the arachnoid villi or the capillary bed and small veins of the pia arachnoid. The perineural channels are probably of little importance under normal conditions. They would appear to be most important below a mechanical block of the spinal subarachnoid space where certainly some fluid is present, and a slow formation and absorption probably takes place.

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Neurology

BOOK REVIEWS

The Diagnosis and Treatment of Convulsive Disorders in Children

Samuel Livingston, M.D. 1954. Springfield, Illinois: Charles C Thomas, Publisher. $9.50.

IN THE preface to this monograph based upon 17 years experience with epileptic children, the author tells his readers he has written this material expressly for the general practitioner. As a guide for the family doctor and the pediatrician, this is an excellent guide to the over-all management of the child with a seizure disorder.

The text provides the reader with knowledge of the conditions associated with symptomatic epilepsy, the use of technical diagnostic procedures (x-ray, electroencephalography, pneumography), excellent discussion of treatment by all the drugs in use at the time of publication, and general management of the epileptic child. An important chapter on the social and psychological management has been contributed by Francis J. Schwentker, and A. Earl Walker has added a chapter on surgical treatment. Conditions that may simulate or be complicated by epilepsy are well reviewed.

The reviewer was disappointed in the cursory treatment of psychomotor seizures. It is true that this form is commoner in adult epilepsy. However, it is a form of focal seizure that may begin in childhood. Often difficult to diagnose, unless the physician is fortified with descriptive material, this form is mistaken for a behavioral or psychotic disorder. An entire chapter might have been profitably devoted to this type of seizure and could have been the background for simple discussion of the neurophysiologic concepts of epilepsy, with the end in view that some day even so-called cryptogenic epilepsy may find its rightful place as symptomatic (organic) in origin. The hereditary or genetic factor in cryptogenic epilepsy may be that of a biologic influence in a lowering of the cerebral threshold for the underlying dysrhythmia.

While the reviewer believes a more detailed description of psychomotor epilepsy would have enhanced the value of the book, its omission is not serious. No doubt the author has purposely limited the description of all seizures, stressing those aspects for which the general practitioner has greatest need.

M.G.M.

NEWSLETTER

JANUARY, 1955

Howard D. Fabing, President
Walter O. Klingman, President-Elect
Francis M. Forster, Vice-President
Alexander T. Ross, Secretary
Dave B. Ruskin, Treasurer

AMERICAN ACADEMY OF NEUROLOGY

President Fabing Inspects Hotel Shamrock

After serving as honor guest at the Western Conference on Epilepsy in Galveston (October 22-23), President Howard D. Fabing visited Houston's famed Hotel Shamrock, which will be the headquarters of the 1955 annual AAN meeting (April 25-30). In Dr. Fabing's words: "This place (the Shamrock) has everything the publicity men have told us. It is a gorgeous hotel with fine accommodations and splendid restaurants. A sheltered walk leads from the hotel to a nearby building which provides an adequate garage on the upper floor and a convention hall, plus display space for exhibits on the first floor.... The big eye-catcher, however, is the beautiful swimming pool and the terrace which flanks it. The hotel manager told me that in April everyone should bring a bathing suit and sun tan lotion to take advantage of the warm Houston sun at this time of year -- a feature which should be of special interest to members who have been snowbound for most of the winter.... The hotel is a few miles south and west of the center of the city and it is very close to Baylor University Medical Center. You will just have to see it to believe it."..... Also while in Houston, President Fabing convened with members of the committee on local arrangements for the 1955 meeting. Chairman of this committee is Abe Hauser, 1119 Lovett Boulevard, Houston, Texas.

Special Review Courses To Precede 1955 Meeting

A. B. Baker, chairman of the AAN committee on special courses, who just recently returned from a lecture tour in the Scandinavian countries, has announced plans for the special courses to be given at the Shamrock Hotel in Houston (April 25-27, 1955), preceding the annual AAN meeting.... Because of constant demand, the courses in neuropathology (Fay Y. Tichy, chairman) and in neurophysiology (James L. O'Leary, chairman) will be repeated. Also to be repeated are courses in electroencephalography (V. R. Zarling, chairman) and neuroroentgenology (A. L. Sahs, chairman). The Academy is fortunate to have again obtained the services of Dr. Harold O. Peterson, who will give the entire course in neuroroentgenology.... Two new clinical courses will be presented, one in collagen diseases of the nervous system and one in neuromuscular disorders. The faculty of the

former will be headed by Joe R. Brown and members of the staff of the Mayo Clinic; the latter will be conducted by G. Milton Shy and other members of the staff of the National Institute of Neurological Diseases and Blindness.... Dr. Baker calls attention to the importance of early registration for these courses. The size of classes must be restricted, and last year many applicants had to be rejected due to late application. Requests for application blanks or further information should be forwarded to Mrs. J. C. McKinley, Executive Secretary, 3501 East 54th Street, Minneapolis 17, Minnesota.

Drs. Woltman and Moersch Honored at Mayo Clinic At the Mayo Clinic on October 16, staff members of the section of neurology in cooperation with the sections of psychiatry and neurosurgery, together with alumni from these sections, convened to honor Henry W. Woltman and Frederick P. Moersch. The program began with a luncheon followed by scientific sessions arranged by Roland P. Mackay in which papers were presented by L. E. Daniels (Denver), John B. Doyle (Los Angeles), Russell T. Costello (Detroit), E. M. Hammes, Jr. (St. Paul), Harold Voris (Chicago), and C. Hunter Shelden (Pasadena). Following the scientific sessions was a social program, written by Alex MacLean, to follow a pattern set by the celebrating Roman legions upon their return from a successful campaign. L. M. Eaton acted as toastmaster and presented to Drs. Woltman and Moersch copies of the book, "Clinical Examinations in Neurology," written by the neurology staff of the Mayo Clinic. The honored guests were then eulogized for their contributions to neurology by Harry L. Parker, John B. Doyle, and Roland P. Mackay. The final ceremony was a presentation to the honor guests of their portraits taken by Yousuf Karsh.

* * * * * *

Prof. G. H. Monrad-Krohn Comments on Neurology in U.S.A. From Prof. G. H. Monrad-Krohn in Oslo, Norway, comes a dispatch of "impressions" on American neurology, gleaned from his visit to this country last summer. Arriving as a guest of the National Multiple Sclerosis Society through the good offices of Hans H. Reese, it was his first visit to the U.S.A. in 27 years.... Referring to efforts of the AAN group to reactivate interest in the practical therapeutic side of clinical neurology at the 4th International Neurological Congress (Paris, 1949), the distinguished professor was particularly anxious to see what had been accomplished since then in this country, where, he says, "things move more briskly than in the impoverished 'old world' of Europe." He was also greatly impressed in this country by "the work done and the opportunities given budding neurologists for a harmonious, neurologic educa-

tion, both on the clinical and basic side, thus avoiding a one-track unbalanced education, too often seen in other countries." Even though coming here with high expectations he still was not disappointed. As he remarks, "A number of new neurologic institutes, clinics, and schools have sprung up in this country, some of them with equipment and opportunities which make a European neurologist rather envious. I had the distinct feeling that the understanding of the importance and needs of neurology are fast gaining ground in the U.S.A. and that the obvious but far from common view that neurology as a discipline should have the same central place in medical research and teaching as the nervous system has in the organism, was beginning to be recognized also outside of neurologic circles." In commenting on the importance of neurology as a central discipline, Prof. Monrad-Krohn referred to the statistics presented by Dr. Kobro (1937) to the Medical Society of Oslo, which indicate that about 50 per cent of the disabled in Norway are the result of various neurologic disorders.... He admired how U. S. interest in neurologic problems has been stimulated by voluntary health organizations such as the National Multiple Sclerosis Society, lauding the leadership of Doctors C. H. Traeger, H. R. Wainerdi, and Miss Sylvia Lawry. As another progressive step, he pointed to the union of constituents from six voluntary health organizations, each one interested in a specific neurologic disorder, into a National Committee for Research in Neurological Disorders.... Also he comments on the progress made in poliomyelitis research and the pioneer work and leadership of neurologists in poliomyelitis; the fact that six Norwegian institutes for the treatment of poliomyelitis are directed by neurologists, as is the French Poliomeylitis Institute at Garches (under Grossiord); the Poliomyelitis Research Unit at Queen Square; and the Radcliffe Infirmary in Oxford (under Ritchie Russell).... Prof. Monrad-Krohn concludes by stating "On the whole, I must confess that I was impressed by the progress made in neurology in the U.S.A. since my last visit -- and equally by the continued activity now going on." He completes his dispatch by saying, "Everywhere I met with a kind friendliness and helpfulness from neurologic colleagues, to whom I am profoundly grateful. Besides meeting the leaders in this field, I enjoyed meeting their many able and courteous assistants and especially seeing again my old friend Dr. Maynard Cohen. We all have pleasant recollections of his long stay in Norway. It was also pleasant to meet my compatriot Sem-Jakobsen at Rochester".... Prof. Monrad-Krohn began his trip at the annual meeting of the American Neurological Association in Atlantic City, and visited neurological centers in New York, Bethesda, Washington, Minneapolis, Rochester (Mayo Clinic), Wisconsin, and Illinois. He regrets that time did not permit him to accept invitations to visit San Francisco and Boston.

Shortage of Neurologists in VA Medical Program Benedict Nagler, chief of the Veterans Administration Neurology Division, reports a shortage of neurologists for the management of the 20,000 neurologic patients now treated each year in VA hospitals and the 5,000 neurologic patients receiving outpatient treatment. This shortage has made it necessary to employ general practitioners as ward physicians on neurologic services in selected hospitals, under the general supervision of trained neurologists. The VA also has plans to have full time VA neurologists visit hospitals where no neurologists are available or where no neurologic consultants can be obtained.... The VA provides residency training programs for prospective neurologists, and in addition, has an on-the-job training program in neurology which provides for full time VA physicians three years of formal residency training plus two years of clinical practice, the latter to be served at stations which are critically short of staff.

Kety Receives Max Weinstein Award The United Cerebral Palsy Max Weinstein award, consisting of a plaque and $1000, was presented to Seymour S. Kety, associate director in charge of research, National Institutes of Neurological Diseases and Blindness and Mental Health, in recognition of his studies on cerebral circulation and cerebral metabolism. The award was made at the annual convention of the United Cerebral Palsy Association, held at the Mayflower Hotel, Washington, D. C. (Nov. 19).

Wartenberg Returns From Freiburg Robert Wartenberg has returned from Freiburg i. Br., where he was guest professor for a half year. He lectured also in Frankfurt, Vienna, Belgrade, and Sarajevo, and read a paper at the meeting of the German Society for Neurology in Wurzburg. At the meeting of the German Society for Neurosurgery in Bad Ischl he was presented with a diploma of honorary membership of this society "for his merits in the development of neurology and international scientific understanding."

G. L. Rasmussen Joins NINDB Staff Dr. Grant L. Rasmussen, professor of anatomy in charge of neuroanatomy at the Medical School of the University of Buffalo, has joined the staff (November 1) of the Laboratory of Neuroanatomical Sciences (under William F. Windle) at the National Institute of Neurological Diseases and Blindness. Dr. Rasmussen, who is well known for his studies of central auditory mechanisms of the brain, will serve as chief of the section on functional neuroanatomy.

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FRANK F. LAW LABORATORY DEDICATED AT TEMPLE UNIVERSITY

The new Frank F. Law Laboratory of the Temple University School of Pharmacy, Philadelphia, was dedicated some six months ago as a living memorial to Mr. Law, who died in 1950. Ceremonies were held in the auditorium of the School of Pharmacy of the university. More than 700 alumni and friends of the school attended the service. Equipment for the laboratory was a gift of Wyeth Laboratories, Philadelphia, of which Mr. Law was a vice-president at the time of his death. Especially equipped to teach the manufacturing of pharmaceuticals, the laboratory will be used in conjunction with a pharmaceutical manufacturing course first offered in the school last fall. In paying tribute to Mr. Law, Harry S. Howard, president of Wyeth Laboratories, said that "no memorial could be more appropriate for Mr. Law who inspired so many others to follow his footsteps into the profession of pharmacy."

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Ansolysen (pentolinium tartrate), a new ganglionic blocking agent, has been introduced by Wyeth Laboratories of Philadelphia. It acts by blocking sympathetic nerve ganglia which decreases peripheral resistance and lowers blood pressure.

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A ready-mixed oral suspension of the penicillin salt of hydrabamine has been introduced by Abbott Laboratories, Chicago. This new preparation marketed under the trade name, Compocillin, remains stable at least 12 months and has an appealing fresh banana smell and taste.

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*Beckman, H. *Treatment in General Practice* (Saunders) 1948.

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GOETCHIUS JOINS AYERST STAFF

Mr. George R. Goetchius has been appointed to the research staff of Ayerst Laboratories, it has been announced by Mr. Boyd O'Connor, president. Mr. Goetchius has done specialized research in the field of antibacterial agents and is responsible for considerable development in the field of quarternary ammonium compounds in industrial sanitation. He received his academic training and an M.S. in bacteriology at Cornell University. He was formerly with the New York State Department of Health, Sterling-Winthrop Research Institute, and Rohm & Hass Company. For seven years he was a member of the disinfectant scientific committee of the Chemical Specialties Manufacturers Association.

BROAD SPECTRUM ANTIBIOTICS

The new broad range antibiotics differ in their activity against specific diseases more widely than has been generally recognized, Henry Welch, Director of Antibiotics of the Food and Drug Administration, told a group of visiting foreign health officers recently at an antibiotics symposium sponsored by Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

"Because of the close similarity of the chemical structure of the tetracyclines there has been a tendency to substitute clinically one for the other on the basis that these drugs have equal antibacterial activity," he warned. He presented laboratory data from Food and Drug Administration laboratories showing how widely Aureomycin (chlortetracycline), Terramycin (oxytetracycline) and tetracycline, the new antibiotic produced by removing a chlorine atom from the molecule of Aureomycin, differ in their effectiveness against various disease germs.

This huge antibiotic industry is only ten years old, Dr. Welch pointed out, recalling that in 1941 there was insufficient penicillin in the United States to treat a single case. Dr. Welch traced the phenomenal rise of antibiotics since World War II. Of 3500 different antibiotic substances isolated and studied since 1942, the great majority have not been found useful because of low potency or high toxicity, but about 15 have proved medically useful.

It has been estimated that in dollars spent for prescription drugs in recent years, conservatively 40 per cent of all prescriptions written include one or more antibiotics. Dr. Welch listed 43 infectious diseases and classes of diseases now controlled by antibiotics, and cited figures to show how they have cut the death toll from many formerly dreaded diseases.

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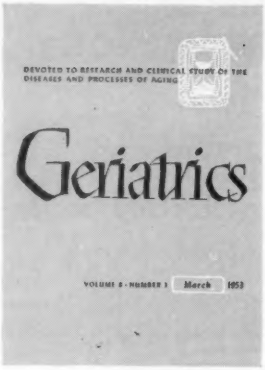

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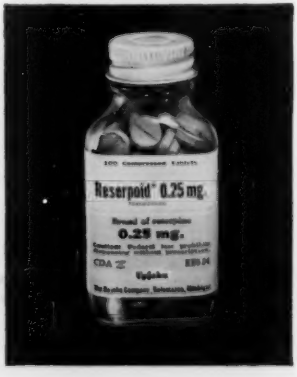

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1. Meller, R. L., and Resch, J. A.: *Bull. Univ. Minnesota Hosp.*, 20:78, Oct. 8, 1948.
2. Meller, R. L., and Resch, J. A.: *Postgrad. Med.*, 6:452, Dec., 1949.

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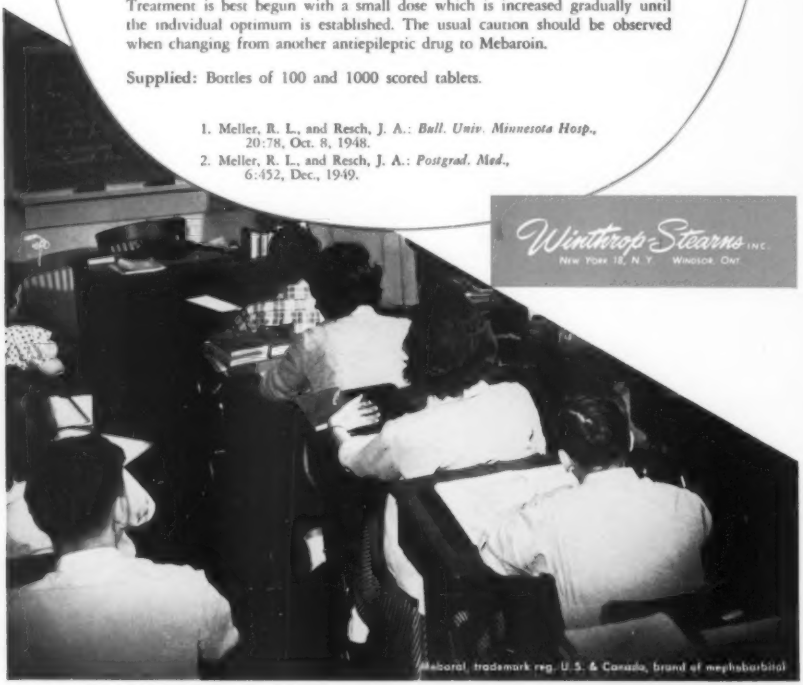

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